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GROWTH STUDIES OF CHILDREN WITH DIABETES MELLITUS *

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Since the beginning of the use of insulin, it has been possible for children with diabetes to approach the status of normal children, in contrast to the marked retardation of development shown previous to its use. A study of the physiologic progress of children suffering with diabetes under the modern regimen should furnish valuable information, and determine whether it is possible for these children to attain maturity with a normal physique.

The information obtained from such a study of the diabetic child should be applicable also to problems concerning the nutrition and development of the nondiabetic child. When the normal person is studied, his many compensatory mechanisms will often mask a response which would be obvious if his margin of metabolic balance were reduced to the minimum, as is the case in children with diabetes. It is well known that children suffering with diabetes, if untreated, react rapidly to adverse conditions by diminution of growth. A regimen which will result in normal development in these children should be even more effective if applied to the nondiabetic child.

During the past five years approximately sixty diabetic children have been observed in this clinic, and thirty-two of these have been studied during repeated periods of hospitalization. The total number of hospital admissions of the various patients is 242. Metabolic studies of various types have been made. The data pertaining to the physical development of these children will be outlined in this article. Other studies will be reported later.

For the past two years, a standardized type [1] of diabetic management has been employed. This should make developmental observations more significant, since the diet for each child has been qualitatively similar, and quantitatively proportional to the degree of physiologic development as determined by the height.

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* Received for publication, Dec. 23, 1927.

* From the Department of Pediatrics, State University of Iowa.

1. Boyd, J. D.: The Use of Standard Diet Formulas in the Control of Juvenile Diabetes Mellitus, J. A. M. A. **87**:1020 (Sept. 25) 1926.

For children over 5 years of age the diet furnishes 1 Gm. of protein for each pound of theoretical weight as determined by the height; for children under 5 years, it furnishes slightly more. Holt and Fales'[2] estimates of energy requirement for full activity were used. In general the fatty acid dextrose ratio was 1½ : 1. It was found advisable to use a ratio of 1¼ : 1, or 1 : 1 for certain periods in the control of four patients of the runabout age. Dietary indiscretions have been extremely infrequent. Since the requirements for full activity have been met, the children do not seem hungry, and the temptation to break diet control is further minimized or entirely avoided by the use of a varied diet.

During the periods of hospitalization, the urine was analyzed daily for sugar and acetone bodies. Twice a week, capillary blood sugar values were determined before breakfast, and two and four hours later, by a micro-modification[3] of the Folin-Wu method. At attempt was made to maintain the blood sugar within normal limits at all times. In the majority of cases, the diurnal fluctuations of the blood sugar values were not appreciably greater than in the normal person.

The patients when discharged from the hospital were advised to return at intervals of from six to twelve weeks for estimations of the blood sugar. Daily routine examinations of the urine were made at home, and a specimen of urine was sent to the laboratory for examination once each week. The degree of cooperation varied, but in general it was satisfactory.

METHOD OF CORRELATION OF DATA

The scope of this report has been limited to observations of degree and rate of growth in height and weight. It was apparent that, as a group, these children were in advance of the standards commonly used, which represent the averages of measurements obtained from large numbers of children. Recent anthropometric studies[4] indicate that the usual standard values of average height and weight are too low for many groups of children. For this reason, we chose as standards values which represented the growth and nutrition of a superior group of children. For the younger group, the average values of the preschool children

2. Holt, L. E., and Fales, H. L.: Food Requirements of Children, Am. J. Dis. Child. **21**:1 (Jan.) 1921.

3. Boyd, J. D.; Hines, H. M., and Leese, C. F.: Study of Response of Continuous Intravenous Injections of Large Amounts of Glucose, Am. J. Physiol. **74**:656 (Nov.) 1925.

4. Gray, H., and Fraley, F.: Growth Standards, Am. J. Dis. Child. **32**:554 (Oct.) 1926. Baldwin, B. T.: Anthropometric Measurements of a Group of Gifted Children. Genetic Studies of Genius, Stanford Univ. Press, 1925, volume one. Faber, H. K.: Variability in Weight for Height in Children of School Age, Am. J. Dis. Child. **30**:328 (Sept.) 1925.

were used;[5] for children over 6 years of age, we employed the values which Baldwin[6] obtained from measurements at the Horace Mann School. These standards make it possible to predict the average height and weight which corresponds to any chronologic age. Similarly, it is possible to determine the average chronologic age corresponding to the child's height. We have used the latter method, and expressed the child's development in terms of deviation in months of the predicted chronologic age from the patient's actual age. The average standard weight value for the patient's height was compared with his actual weight, and the deviation expressed in per cent of the standard.

PRESENTATION OF DATA

Developmental Status at Onset.—It seems probable that potential derangement of metabolism frequently exists prior to the onset of diabetic symptoms. For this reason, it is of interest to study the physical characteristics of the children at the first manifestations of the disease.

Chart 1 shows the measurements of twenty diabetic patients made not later than three months after the recognized onset of the condition. Most of these were obtained within from three to fourteen days after the onset of obvious symptoms.

Of twenty patients, fifteen were overheight for their age. The average advance of the predicted over the actual age was 8.4 months. Five patients were below the standard, with an average retardation of six months. A survey of the entire group showed an average advance of 4.8 months over the chronologic age. Five patients were overweight for their height; the average deviation was 11.56 per cent; fifteen were underweight, with an average deviation of 12.15 per cent. The whole group averaged 6.2 per cent underweight for their height. It is of interest to note that none of the underheight group was overweight.

Ladd,[7] in a similar study, found that thirty-one of thirty-five diabetic children at the onset of the disease were either overheight or overweight, or both, for their age. The standards of weight which he used (Stratz)[8] were about 7.5 per cent, and the height standards about 3 per cent lower than those which we have employed. An interpretation

5. Baldwin, B. T.: The Physical Growth of Children from Birth to Maturity, University of Iowa Studies, Studies in Child Welfare **1**:60 (June) 1921.

6. Baldwin (footnote 5, pp. 261, 280, 294 and 310).

7. Ladd, W. S.: Growth in Children with Diabetes Mellitus, Am. J. Dis. Child. **32**:812 (Dec.) 1926.

8. Stratz, C. H.: Wachstum und Proportionen des Menschen vor und nach der Geburt, Arch. f. Anthropol. **8**:287, 1909.

of his statistics in terms of our standards indicates that the developmental characteristics of the two groups were similar at the onset of the disease.

If the group is studied as a whole, it might be said that the average of these diabetic patients, at the time the disease became manifest, was slightly overheight for his age, and underweight for his height. The extent of these deviations is not greater than is often encountered in many apparently normal children. There are some individual variations of height which are worthy of note. More of these occurred during

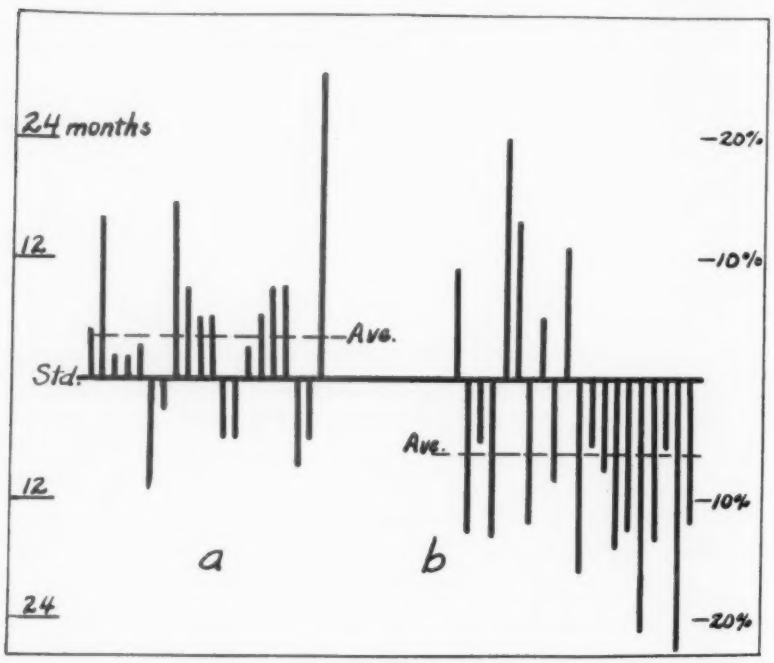

Chart 1.—Deviation of height and weight from standard values, at onset of manifest diabetes. Deviation of each child is expressed by a vertical line and the average deviation by a horizontal dotted line. Height deviation (*a*) is expressed as the difference in months between the actual chronologic age, and the age predicted from the patient's height. Weight variation (*b*) is expressed as percentage deviation of the patient's weight from the standard weight value for his height.

the periods of normal rapid growth, early and late childhood, than during the intermediate period. It should also be kept in mind that a loss of weight may occur more quickly than an arrest of growth in height. It is possible that these children were not underweight when the break of metabolic compensation occurred.

Rate of Growth.—Table 1 presents a summary of the first and last measurements of thirty-two diabetic children who were under observation for varying periods of time. Approximately one half of these

TABLE 1.—*Summary of Average Initial and Terminal Deviations of Height and Weight from the Standards used in this Study.**

	Apparent vs. Chronologic Age						Percentage Deviation of Weight					
	Retarded		Advanced		Total		Underweight		Overweight		Total	
Time of Observation	No. Cases	Mo.	No. Cases	Mo.	No. Cases	Mo.	No. Cases	%	No. Cases	%	No. Cases	%
First observation.....	11	−8.8	21	+10.3	32	+3.8	19	−11.4	11	+ 8.0	32	−4.0
Last observation.....	13	−7.7	19	+13.0	32	+4.6	5	−10.3	23	+10.3	32	+5.8

* The former is expressed as the difference in months between the apparent age as determined by height and the chronologic age. Weight is expressed as precentage deviation from the standard for the patient's height.

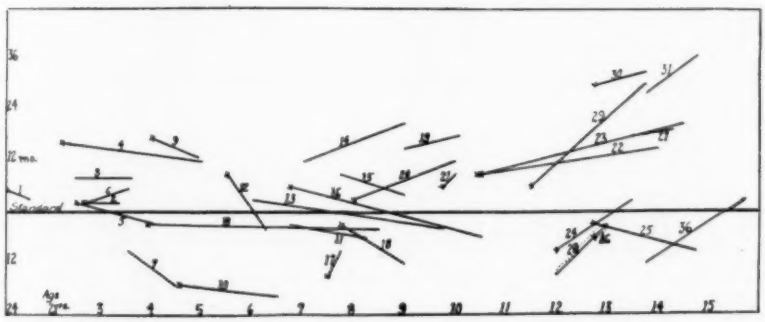

Chart 2.—Deviation of height at initial and terminal observations expressed as difference in months between the actual chronologic age and the age predicted from the patient's height. The age of the patient at the time of the observation is expressed horizontally, deviation from chronologic standard vertically. The numbers correspond to the serial numbers of the patients included in this study. Those values indicated by a cross (*x*) were obtained soon after the diabetes first became manifest.

patients had been under diabetic control for several months before the first values were obtained. The time interval between the first and last measurements varied from three months to four and one-half years, with an average interval of 1.6 years. Eleven children had been under observation for more than two years.

Individual progress is shown in chart 2, which presents the deviation in months from the chronologic age at the first and last observation.

Of eighteen patients whose first measurements showed them to be three months or more ahead of their chronologic age, only three failed to maintain this status. Ten not only maintained their advanced status, but increased it.

TABLE 2.—*Summary of Initial and Terminal Measurements of Thirty-Two Diabetic Children**

Number of Patient	Initial Measurements						Terminal Measurements					
	Height, Cm.	Actual Age	Calculated Age	Deviation, Months	Actual Weight, Kg.	Calculated Weight, Kg.	Deviation, per Cent	Height, Cm.	Actual Age	Calculated Age	Deviation, Months	Actual Weight, Kg.	Calculated Weight, Kg.	Deviation, per Cent
1.....	78.7	12 months	17 months	5	9.5	10.4	9.0	82.4	18 months	21 months	3	13.0	11.3	15.0
2.....	92.2	32 months	34 months	2	12.7	13.4	— 5.2	96.1	40 months	42 months	2	14.0	14.0	0.0
3.....	93.9	29 months	37 months	8	13.0	14.0	— 7.1	101.6	43 months	51 months	8	16.7	16.0	4.3
4.....	96.6	26 months	42 months	16	12.7	14.6	—13.0	115.6	60 months	72 months	12	21.0	20.5	7.3
5.....	90.1	29 months	31 months	2	14.5	12.0	20.0	99.0	48 months	45 months	— 3	19.0	15.0	26.6
6.....	91.9	32 months	34 months	2	15.1	13.4	13.0	99.6	42 months	47 months	5	18.1	15.3	18.2
7.....	90.1	42 months	31 months	—11	12.4	12.0	3.3	93.2	53 months	36 months	—17	16.2	14.0	15.7
8.....	99.1	47 months	44 months	— 3	13.3	15.1	—11.9	127.0	8½ years	8¼ years	— 3	25.5	25.0	0.8
9.....	108.0	48 months	65 months	17	18.4	17.5	5.0	115.7	59 months	72 months	13	23.6	20.5	10.2
10.....	94.0	54 months	37 months	—17	15.0	14.0	7.1	104.7	6¼ years	56 months	—20	17.9	16.7	7.2
11.....	116.8	6¾ years	6½ years	— 3	20.8	20.8	0.0	123.1	8¼ years	7¾ years	— 6	29.0	24.4	18.8
12.....	114.3	5½ years	6¼ years	9	18.3	20.0	— 8.5	117.0	6¼ years	6¾ years	— 6	22.0	21.0	4.7
13.....	113.5	6 years	6¼ years	3	20.0	19.5	2.5	130.2	9¾ years	9½ years	— 3	32.3	27.0	19.6
14.....	127.0	7 years	8 years	12	25.2	24.4	3.2	139.7	9 years	10¾ years	21	32.4	32.9	— 1.5
15.....	127.0	7¾ years	8½ years	9	27.1	26.0	4.2	132.1	9 years	9¼ years	3	34.4	28.0	21.4
16.....	121.9	6¾ years	7¼ years	6	18.6	22.2	—16.0	134.6	10½ years	10 years	— 6	32.1	30.0	7.0
17.....	120.6	7½ years	6¾ years	—15	21.0	22.1	— 5.8	121.6	7¾ years	7 years	— 9	23.1	23.1	0.0
18.....	121.7	7¾ years	7¼ years	— 3	20.5	22.2	— 7.6	124.4	9 years	8 years	—12	25.4	24.4	4.6
19.....	137.2	9 years	10¼ years	15	32.2	31.0	3.5	144.7	10 years	11½ years	18	38.5	36.9	4.3
20.....	127.0	8 years	8¼ years	3	21.8	25.3	—14.0	140.2	10 years	11 years	12	35.6	33.7	5.6
21.....	138.9	9¾ years	10¼ years	6	27.5	31.5	—12.7	139.7	10 years	10¾ years	9	42.3	32.4	30.5*
22.....	142.2	10½ years	11¼ years	9	27.2	34.5	—21.0	166.4	14 years	15¼ years	15	53.0	52.2	21.0
23.....	142.8	10½ years	11¼ years	9	29.9	34.5	—13.3	164.7	14¼ years	16 years	21	51.8	54.6	— 4.7
24.....	142.7	12 years	11¼ years	— 9	32.5	34.5	— 5.8	156.4	13½ years	13¾ years	3	50.3	48.2	4.3
25.....	149.1	12¾ years	12½ years	— 3	45.4	42.4	16.5	157.5	14¾ years	14 years	— 9	49.5	49.1	0.0
26.....	129.8	12¾ years	12¼ years	— 6	31.0	40.0	—22.5	151.0	13 years	12¾ years	— 3	39.8	43.0	—15.8
27.....	159.3	13½ years	15 years	18	51.5	51.5	0.0	160.3	14¼ years	16 years	21	55.4	54.6	1.4
28.....	139.7	12 years	10¾ years	—15	31.4	33.0	— 4.8	146.6	13 years	12¾ years	— 3	35.6	39.4	— 9.3
29.....	144.7	11 years	11½ years	6	34.5	36.9	— 6.5	165.2	13¾ years	16 years	30	56.6	54.6	3.6
30.....	163.8	12¾ years	15¼ years	30	46.1	52.5	—12.0	173.2	13¾ years	16½ years	33	57.7	56.6	1.9
31.....	160.0	13¾ years	16 years	28	39.2	54.6	—28.2	160.0	14¾ years	16 years	15	43.5	54.6	—20.3
32.....	149.8	13¾ years	12¾ years	—12	38.6	39.6	— 1.0	166.3	15¾ years	15½ years	3	54.2	54.4	0.0
								142.2	10¼ years	11¼ years	12	41.5	34.7	19.5
Average deviation				+3.4 months			— 4.0%				+4.7 months			+ 5.8%

* Later observation.....

* The calculated age and weight are the values corresponding to the patient's height, according to the standards of measurement used in this study. The deviation of the patient's actual age and weight from these standards is expressed in terms of months and percentage, respectively.

Of eleven patients who at the time of the first observation were three months or more below their predicted development, two were in advance of this development after intervals of eighteen months and two years, respectively. The growth curve of three others is rapidly approaching the standard. Five of these patients, after from one to two years of treatment, were further below the standard than at the time of their first observation. Eleven children, at the time of the last measurement, were one year or more in advance of their chronologic age; three showed a retardation of one year or more.

Nineteen patients were underweight at the time the first measurement was obtained; five were underweight at the time of the last observation. The average weight of the group at the first observation was 4 per cent below the standard for height. The average of the final values was 5.8 per cent overweight for height. Nine children were more than 10 per cent overweight, and four of these were also underheight. A summary of the data for each patient is given in table 2.

COMMENT

So far as can be determined by measurements of height and weight, the majority of this group of diabetic children are growing at a satisfactory rate. The average rate of growth is superior to the averages obtained from observations made on selected groups. We do not know the optimum rate of growth. It certainly cannot be determined solely by acquisition of height or weight or both. It must be correlated with other evidences of physiologic progress. If the latter can be demonstrated, then rapid growth in height would seem to be an indication of adequate control of the exogenous factors which influence growth.

If it is possible to cause a diabetic child to develop physically as a nondiabetic child without increasing the severity of his disease, this and nothing short of this should be our goal. Increase of tolerance as indicated by a diminution of the insulin requirement has been the rule in the treatment of these patients.

Our data would indicate that six children are retarded three months or more in growth and are not growing at the average rate. When the heights of these children are interpreted according to other standards (Stratz, Wood), cases 13 and 16 fall within normal limits. However, these two patients have shown persistent hyperglycemia and frequent glycosuria due to inadequate insulin regulation while at home. The other four show definite physical retardation. This small group of patients who have not maintained average growth merits more detailed consideration in order to determine, if possible, the cause of the retardation.

Diabetic control has not been satisfactory in five of these children. In two (cases 13 and 16), there was inadequate cooperation at home.

Three patients (cases 7, 10 and 11) have shown marked lability of the sugar-handling mechanism, oscillating at all times between glycosuria and hypoglycemia. This in itself is probably an adequate explanation for the poor status of these patients. Four patients (cases 7, 10, 11 and 18) were definitely retarded at our earliest observation. This suggests that the cause of their retardation is deep-seated, and that possibly the diabetes is a further manifestation of the same basic deficit. One child (case 18) has a definite enlargement of the thyroid gland.

Our observations and those recorded by others [9] would indicate that diabetes in itself is not incompatible with normal growth, providing the control is such that prolonged or repeated hyperglycemia is avoided and the child's nutritional requirements met by an adequate diet.

Joslin's [10] observations are less encouraging. He has presented statistics of the growth of twenty patients who had been under insulin management for thirty months. The gain in weight was slightly above the average gain predicted by the standards. The increase in height, however, was less than one half of the predicted increase for that period. Eleven of the children presented in this study have been under insulin management for two years or more. The average growth in this group is about 20 per cent in advance of the average normal increase for children of similar ages. The average increase in weight is even higher in comparison. One outstanding difference between the type of management employed by Joslin and that used in this clinic is the energy equivalent of the diet. The children concerning whom a report is made in this study were fed a diet [11] calculated to provide for full activity, while Joslin's [12] children received from one half to three fourths of this amount.

The character of the growth in these patients is apparently normal. Without exception, the children appear vigorous and healthy, and seem out of place in a ward of sick children. The nutritional state as indicated by the weight appears satisfactory. The majority do not show visual evidence of being overweight for height. The few that tend toward obesity are those whose control has been inadequate or of brief duration.

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9. Ladd (footnote 7). Boyd, G.: The Treatment of Diabetes in Children, Am. J. Dis. Child. **29**:329 (March) 1925. Hartman, A. F.: Diabetes Mellitus in Infants and Children. M. Clin. N. Amer. **9**:69 (July) 1925.

10. Joslin, E. P.; Root, H. F., and White, P.: The Growth, Development and Prognosis of Diabetic Children, J. A. M. A. **85**:420 (Aug. 8) 1925.

11. Boyd, J. D., and Nelson, M. V.: Diabetic Diets for Children, J. Am. Dietetic Assn. **2**:45 (June) 1926.

12. Joslin, cited by Gray, H.: Diabetic Children's Diets in Different Clinics, Am. J. M. Sc. **172**:394 (Sept.) 1926.

During the first few months after the dietary management has been established, the gain in weight is often out of proportion to the gain in height. If the management is adequate, growth of height is accelerated, and the patient's proportions soon tend to approach the standard.

SUMMARY

This study, in confirmation of similar observations by others, indicates that if uncomplicated diabetes mellitus is adequately controlled, it does not prevent satisfactory growth.

Such control implies approximation and maintenance of normal blood sugar values and an adequate diet.

The growth response of these carefully regulated diabetic children is greater than that of so-called superior groups of nondiabetic children.

This would suggest that the present concept of the rate of normal development for a healthy child may not equal his optimum, and that this might be better approximated by careful dietary regulation throughout childhood.

Part of the data presented in this article was obtained by Miss Idel Pyle, of the Child Welfare Research Station, Iowa City, Iowa.

SCARLET FEVER

II. THE DEVELOPMENT OF TOXIN SENSITIVITY OF THE SKIN IN INFANTS AND ITS RELATION TO THE PRESENCE OF ANTITOXIN IN THE BLOOD*

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In a previous paper,[1] it was shown that skin sensitivity to scarlatinal streptococcus filtrate toxin was present at birth in only a small number of infants, and that in most infants up to 3 months of age, the skin did not react to a considerable amount of the toxin. This lack of skin sensitivity was not entirely due to the presence of antitoxin, since many such infants without a demonstrable amount of antitoxin in the blood had negative skin reactions between one and three months after birth. Those without antitoxin at birth, however, developed some skin sensitivity to the toxin within three months in a larger percentage than those in whom antitoxin was demonstrable.

The present paper deals with a study of the skin sensitivity to toxin during later infancy and childhood. It was not possible to follow up the same infants tested at birth except in occasional instances, but groups of persons at various age levels were studied in an attempt to trace the development of the skin sensitivity and its relation to antitoxin in the blood. The infants and children tested were, for the most part, healthy. They include those from a municipal health clinic and many from the Shriner's Hospital for Crippled Children who were under treatment for orthopedic conditions. Some from the St. Louis Children's Hospital were suffering from minor infections of various types. In general, they represent a typical group of children of the middle and poorer classes of St. Louis. The only selection made was that none was included into whom blood had been transfused, nor any who had scarlet fever or who had recently recovered from it.

The methods used were the same as those described in the previous report. All skin tests were made with 2, 20 and 50 standard skin test doses (STD) of a scarlatinal filtrate toxin which contained 100,000 STD per cubic centimeter. Antitoxin was determined by neutralization tests

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* From the Department of Pediatrics, Washington University School of Medicine, and the St. Louis Children's Hospital.

1. Cooke, J. V.: Scarlet Fever: I. The Relation Between Antitoxin in the Blood and Skin Sensitivity to Toxin in New-Born Infants and Their Mothers, Am. J. Dis. Child. **34**:969 (Dec.) 1927.

and by the intradermal injection of 0.5 cc. of serum in fresh scarlet fever rashes. Usually these two methods agreed qualitatively when used on the same serums, although occasionally there was definite rash-blanching by a serum in which the neutralization test was read negative. This was interpreted to indicate that the blanching test was somewhat more delicate quantitatively.

The reaction of the skin of the same person to varying amounts of toxin and the appearance of the tests may be mentioned briefly, since variations in the size and appearance of the reactions occurred. In appearance, the positive reactions varied from a pink erythema to a rather bright red, and were always well defined and measurable. Not infrequently faint, "ghost" type reactions were observed which were almost invisible in a bright light, but which were plainly outlined when shaded or when the skin was wiped gently with an alcohol sponge. The intensity of the reaction in the same subject was usually more marked when a larger amount of toxin was used. Even with large skin doses, however, there was never any vesication or change in character of the reaction, although the area involved was larger. The marked reactions with larger amounts of toxin often persisted for from two to four days, fading gradually and leaving faintly pigmented outlines. Positive reactions were noted at times to fade relatively quickly when exposed to direct sunlight. In certain instances in which positive reactions appeared large, swollen and confluent, and resembled pseudo-Schick tests, control tests with the same amount of toxin heated to 100 C. for two hours were performed, but the results were always negative.

The size of the positive reactions was usually from 10 to 20 mm., although often those resulting from the larger amounts of toxin were from 30 to 40 mm. in diameter. Only a relatively small number reached a diameter of from 50 to 60 mm. In recording the reactions, only those which reached a diameter of 10 mm. were called positive. Smaller areas occasionally noted were possibly the results of slight reactions, but these reactions were classed as negative; otherwise all negative tests showed nothing but needle tracks. A slight superficial induration, 10 mm. or less in diameter, could usually be palpated at the site of negative tests even though a visible change in the skin could not be seen. All tests were read after approximately twenty-four hours and the measurements recorded.

It should be mentioned again that all children giving positive skin reactions are not suitable for toxin neutralization tests, since in some persons serum without antitoxin, when mixed with toxin, inhibits the reaction. For this reason, only those who show by preliminary tests that nonblanching, antitoxin-free serum gives a positive skin test when mixed with toxin, can be employed. Each serum was tested on four children, and necessary controls were always included.

In more than 100 children the effect of intradermal injections of filtrate heated for two hours to 100 C. was compared with the skin reactions obtained from the unheated filtrate in the same dilutions. The results are of some interest and will be summarized. The heated filtrate was used in 0.1 cc. amounts of dilutions of 1 : 5,000, 1 : 500 and 1 : 200, which corresponded to 2, 20 and 50 STD of the unheated toxin. In the majority, a reaction was not noted, even when the lowest dilution (1 : 200) of the heated preparation was used. There were a few instances, however, in which 0.1 cc. of this dilution gave a definite reaction of 10 mm. or more in diameter. These were of the same type as those given by unheated filtrate. In a group of children who gave such positive skin tests to heated filtrate, the effect of higher temperatures was also noted. Filtrate in a dilution of 1 : 200 was autoclaved for periods varying from fifteen minutes to four hours at 20 pounds (9 Kg.) pressure, and 0.1 cc. injected intradermally. It was found that while heating at the higher temperatures inhibited the skin reactive substance of the filtrate for some children, in others, positive reactions were obtained even with the filtrate autoclaved four hours. Attempts to neutralize this skin reactive substance in the heated toxin by serum which contained antitoxin were unsuccessful. These results indicate that lower dilutions of such streptococcus filtrate contain a substance which reacts with the skin of certain persons and which differs from the neutralizable toxin. It is probable that some of the children in the series here reported as giving reactions only to 50 STD of the toxin were of this nonspecific type. This does not apply to all such reactions, since in the control series many that reacted with 50 STD of the unheated filtrate did not give any reaction to the heated preparation. It would seem, however, that in general, tests performed with lower dilutions of filtrates should be supplemented by additional tests with a heated control in order to exclude nonspecific reactions. The advantage of a potent filtrate is obvious.

This substance may be the same as that described by Mackenzie and Hanger [2] as giving skin reactions in human beings with from 0.03 to 0.04 cc. of undiluted filtrates of hemolytic streptococci and other organisms, and with that studied by Mackie and McLachlan [3] in an induced sensitiveness of the skin in guinea-pigs. In both these investigations, the filtrates were not inactivated by heating, were not neutralizable and were apparently not specific for hemolytic streptococci.

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2. Mackenzie, G. M., and Hanger, F. M., Jr.: Allergic Reactions to Streptococcus Antigens, J. Immunol. **13**:41 (Jan.) 1927.

3. Mackie, T. J., and McLachlan, D. G. S.: Experimental Sensitization to Culture Filtrates of Streptococcus Scarlatinae, Brit. J. Exper. Path. **8**:129 (April) 1927.

In table 1 are collected the results of tests made on 1,240 children from 1 month to 16 years of age, together with the results from 200 new-born infants and 200 mothers previously studied.[1] The infants have been divided into fractional year groups and the older children into year groups. The actual numbers tested and those giving positive skin tests to 2, 20 and 50 STD are shown, as well as the number giving negative tests to 50 STD.

In order to illustrate the differences in skin sensitivity to scarlatinal toxin at different ages, the results from table 1 are charted graphically

TABLE 1.—*The Degree of Skin Sensitivity to Scarlatinal Toxin at Different Ages*

		Skin Reactions							
		+ 2 STD		+ 20 STD		+ 50 STD		− 50 STD	
Age	No. Tested	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Birth	200	2	1	10	5	16	8	172	86
1-3 Months	127	8	6	18	14	15	12	86	68
3-6 Months	43	2	5	11	26	6	14	24	55
6-9 Months	54	19	35	19	35	7	13	9	17
9-12 Months	47	26	55	14	30	3	6	4	9
1-1½ Years	77	59	77	14	18	1	1	3	4
1½-2 Years	53	36	68	13	24	2	4	2	4
2-3 Years	49	32	65	7	14	5	10	5	10
3-4 Years	51	32	62	7	14	5	10	7	14
4-5 Years	41	26	63	5	12	3	7	7	18
5-6 Years	54	30	56	7	13	6	11	11	20
6-7 Years	74	28	38	13	17	9	12	24	33
7-8 Years	65	21	32	14	21	11	17	19	30
8-9 Years	73	25	34	10	14	16	22	22	30
9-10 Years	85	30	35	17	20	11	13	27	32
10-11 Years	74	29	39	11	15	12	16	22	30
11-12 Years	75	27	36	18	24	10	13	20	27
12-13 Years	56	16	29	16	29	10	18	14	25
13-14 Years	72	17	23	20	28	14	20	21	29
14-15 Years	70	17	24	20	29	14	20	19	27
Adults	200	53	27	54	27	42	21	51	25
Total	1640								

by percentages in chart 1. Although it seems probable that the analysis of larger age groups might show minor variations in percentages, the numbers tabulated are sufficient to emphasize the rather striking variations that occur at certain periods in childhood.

The relatively slow development of skin sensitivity in infancy is well illustrated by the age curves in chart 1. Although at birth a small proportion of infants show a skin sensitivity to even large amounts (50 STD) of toxin, during the next six months there is a marked increase in the number reacting to larger doses, even though the number who have become sensitive to a small dose remains small. In infants more than 6 months of age, there is a relatively sudden and striking increase in skin sensitivity not only to larger amounts of toxin but also

to small doses. This increase in skin sensitivity continues and is most marked during the second year, after which there is a slight gradual decline until the age of 6. At this point there is a sudden decrease in sensitivity, which drops again during the next year to reach a level which varies only slightly during the rest of childhood and which is approximately the same as for adults. In general, the curves of sensitivity to 20 and to 50 STD of toxin are of a character similar to that of 2 STD.

It has not been possible to carry out successive tests at intervals on many infants to show the individual development of skin sensitivity in later infancy. In a certain number of instances, however, tests repeated at intervals of several months on the same infants have shown increased skin sensitivity to toxin in later tests. For example, certain infants who gave negative reactions to 50 STD, or negative to 20 STD and positive reactions to 50 STD of toxin in early infancy, were found to give posi-

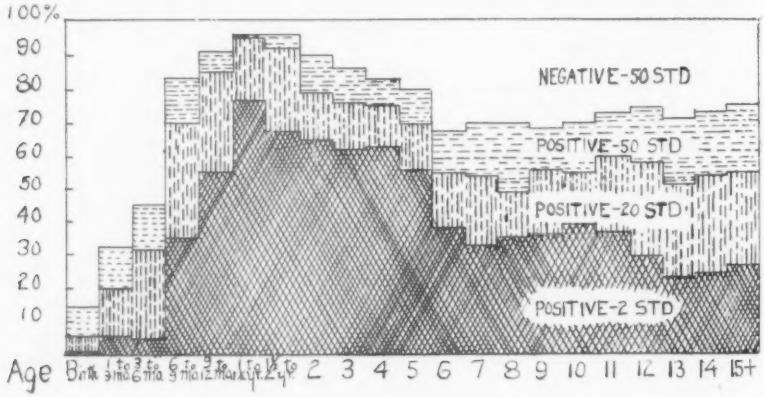

Chart 1.—Relation of skin sensitivity to age.

tive reactions to 2 STD in later infancy. This was, of course, expected from the differences in sensitivity in later infancy shown in chart 1.

Particular interest centers in those children whose skin is not sensitive to a relatively large amount (50 STD) of filtrate toxin and the relation of this lack of skin sensitivity to age. It will be seen (chart 1) that at birth most infants have skins insensitive to this large dose of toxin, and that the number of such persons decreases markedly after six months as skin sensitivity develops. During the second year, less than 5 per cent fail to react, and after this time, there is a gradual increase in such "immune" children to approximately 30 per cent during later childhood.

A comparison of the percentage curve of positive Dick tests at various ages (1 STD) from chart 1 with those of other observers shows that they are similar. This will be seen in chart 2, in which the figures of

Zingher [4] (New York), von Bókay [5] (Hungary) and Malmberg and Jacobsohn [6] (Stockholm) are also plotted. The gradual development of skin sensitivity during the first year, however, is not evident in the other figures because of the age groupings tabulated. Another factor must be taken into consideration in analysis of skin sensitivity of young children. There may be a marked difference in results obtained in infants and young children who are in close contact in nurseries and asylums, when compared with those of the same age in isolated homes. Evidence on which this statement is based will be reported subsequently. In the figures of other observers already mentioned, the decrease in skin sensitivity, as shown by the Dick test in older children, is somewhat less marked at the beginning of the school age, although the correspondence of the curves is close.

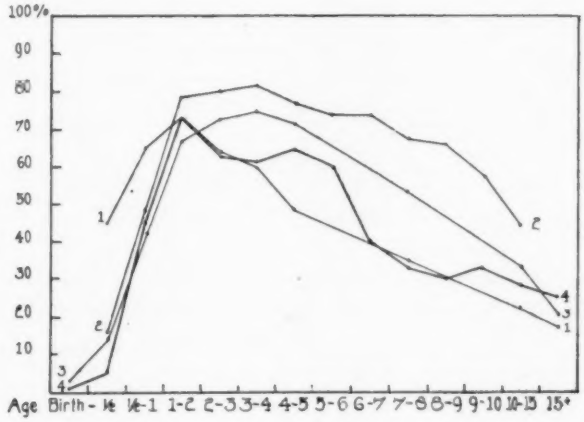

Chart 2.—A comparison of the percentage curves of positive Dick tests at various ages. Curve *1* represents the results of Zingher (New York) in 7,700 cases; *2*, those of Malmberg and Jacobsohn (Stockholm) in 1,200 cases; *3*, those of Bókay (Hungary) in 7,431 cases, and *4*, our results in 1,640 cases.

Some observations were made on the effect of an attack of scarlet fever some years previously on the skin sensitivity, although in many instances a reliable history was not obtainable. A definite history of the disease was obtained in only sixty-four children over 3 years of age. Of these, nine (14 per cent) gave positive reactions to 2 STD; eighteen (28 per cent) to 20 STD, and eleven (17 per cent) to 50 STD; twenty-

4. Zingher, A., quoted by Park, W. H.: Scarlet Fever, Etiology, Prevention by Immunization and Antitoxin Treatment, J. A. M. A. **85**:1180 (Oct. 17) 1925.

5. Von Bókay, J.: Ueber de Bekämpfung des Scharlachs mittels des Dicksche Hautreaktion bei Kindern, Monatschr. f. Kinderh. **34**:294, 1926.

6. Malmberg, N., and Jacobsohn, G.: Einige Untersuchungen über die Dicksche Reaktion im Kindesalter, Acta. Paediat. **6**:442 (May 28) 1927.

six (41 per cent) gave negative reactions. This corresponds with other reported observations that all children who have had scarlatina do not give a persistently negative reaction to the Dick test, although the degree of skin immunity in this small series is greater than that shown by all children tested between 6 and 15 years of age. In only seven instances were children who had had previous tests observed to contract scarlet fever. Of these, six had had positive reactions with 2 STD, while one had given a negative reaction with 2 and a positive reaction with 20 STD.

The relation of demonstrable antitoxin in the blood to the differences noted in skin sensitivity has been further studied.

RELATION OF ANTITOXIN TO VARIATION IN SKIN SENSITIVITY

In a previous paper,[1] it was shown that many new-born infants who gave negative skin reactions to as much as 50 STD did not have demonstrable antitoxin in the blood, and it was therefore considered that in such infants the negative tests were to be regarded as a lack of skin sensitivity rather than immunity. In mothers with negative tests, on the other hand, antitoxin was readily demonstrable. For this reason, a study was made of the presence of demonstrable antitoxin in the blood of a number of normal persons at various ages and with varying degrees of skin sensitivity to scarlatinal toxin. The results of the antitoxin determinations on 167 persons are given in table 2. These include fifty-four new-born infants and twenty adults reported previously. They have been divided into age groups, and the degree of skin sensitivity of the subjects tested is shown. The subjects were selected at random and were clinically free from acute infections. Tests for antitoxin were made as previously described.

TABLE 2.—*Relation of Antitoxin in the Blood to Skin Sensitivity to Scarlatinal Toxin at Various Ages*

		Skin Reactions							
		+ 2 STD		+ 20 STD		+ 50 STD		−	
		Antitoxin		Antitoxin		Antitoxin		Antitoxin	
Age	No.	+	−	+	−	+	−	+	−
New-born	54	0	1	0	3	1	5	26	18
2-6 Months	9	.	.	0	1	0	1	3	4
6-12 Months	8	0	2	0	2	0	1	1	2
1-2 Years	4	0	1	.	.	.	.	2	1
2-6 Years	15	0	3	2	0	4	0	6	0
6-10 Years	20	1	10	3	1	3	0	2	0
10-15 Years	29	2	14	3	2	1	0	7	0
Adults	28	1	10	4	1	6	0	6	0

It will be seen from table 2 that during the first two years of life, as in the new-born, a negative skin test did not indicate the presence of

demonstrable neutralizing antitoxin in the blood. Antitoxin could not be found in a number of infants even though the skin reaction was negative to considerable amounts (20 and 50 STD) of toxin. Although in the first two years, all infants who gave a negative skin test with 2 and 20 STD of toxin did not show demonstrable blood antitoxin, the actual number examined was relatively small (five), and it is probable that if more had been tested, some would have been discovered who had antitoxin. The fact to be emphasized, however, is that in infants up to 2 years of age, the absence of skin sensitivity to toxin is not necessarily dependent on the presence of antitoxin in the blood. In contrast to infants, it will be seen that in children more than 2 years of age, antitoxin was constantly demonstrable in those whose skin was negative to 20 STD of toxin or more. It will be noted that in four of sixteen older children and adults who gave positive reactions to 20 STD, antitoxin was not found. Of these four, two gave positive skin reactions to 5 STD, although they were negative to 2 STD. The other two were not tested with intermediate doses. It seems likely that in such instances, any antitoxin present is present in small amounts and is not demonstrable by the method used.

The presence of demonstrable antitoxin in the blood of certain persons whose skin is sensitive to small amounts (2 STD) of toxin, as shown in four of forty-one persons over 2 years of age, was unexpected and may represent some type of pseudoreaction. The results in all four were verified by additional tests. In each of these instances, however, the intradermal injection of toxin heated to 100 C. for two hours did not give a reaction. The serum of two of the subjects not only gave positive neutralization tests, but blanched an early scarlet fever rash locally in doses of 0.5 cc. The other two serums gave negative neutralization tests, although the blanching tests were positive. One of the children gave a history of having had scarlet fever. A similar observation of positive skin tests and the presence of antitoxin in the blood has been reported by Davies [7] in tests on persons some months after an attack of scarlet fever, and Frenkel and Margolis [8] also noted positive Schultz-Charlton tests with serum from two children who gave positive reactions to the Dick test. Apparently, in a certain small percentage of persons who have a positive skin reaction to a small amount of scarlatinal toxin, antitoxin is demonstrable in the blood. There is no evidence that this is a pseudoreaction, since with heated control tests, the reactions are negative.

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7. Davies, J. A. V.: Studies in Scarlet Fever: IV. Post-Scarlatinal Immunity in Patients Treated with Antitoxin, J. Clin. Investigation **3**:423 (Dec.) 1926.

8. Frenkel, H., and Margolis, A.: Untersuchungen über die Dicksche Hautreaktion bei Kindern, Ztschr. f. Kinderh. **41**:302, 1926.

COMMENT

The relative absence of skin sensitivity during early infancy and the rather gradual development of this property later might have several possible explanations. The assumption of an inherited antitoxic immunity from the mother in early life which disappears later might account for the phenomenon in a certain proportion of cases, but, as shown previously,[1] does not explain the considerable number in whom demonstrable antitoxin is not present. Zingher[9] referred to "the limited ability of the skin of young infants to respond to inflammatory stimuli" as an explanation for the relative lack of reactivity in young infants. Even the youngest infants' skins, on the other hand, respond with considerable intensity to such inflammatory stimuli as erysipelas, pemphigus, heat and trauma; in addition, the lack of reactivity to scarlatinal filtrate toxin persists in many instances for several months.

The possibility that the skin sensitivity is dependent on an acquired hypersensitivity to streptococcus protein must also be considered. Hemolytic streptococcus infections of the upper respiratory tract are extremely prevalent in infancy, and the opportunity for such a sensitization in early life is therefore present. If sensitization to bacterial protein can occur, the observation of the gradual development of skin reactivity in later infancy would seem to be in harmony with such a process.

The decrease in skin sensitivity in later childhood is apparently associated with the presence of specific neutralizing antibody (antitoxin) in the blood. This immunity is probably acquired as a result of later streptococcic infection. It has been repeatedly demonstrated that the injection of small, but increasing amounts of scarlatinal streptococcus filtrate toxin into children whose reaction to the Dick test is positive is followed by a negative reaction to this test and the development of antitoxin in the blood. Unless considerable amounts of toxin are injected, a rash does not occur. If a skin immunity can be induced artificially by the gradual introduction of toxin without the production of a rash, it seems likely that a similar immunity could occur as a result of subacute low grade hemolytic streptococcus infections in which the toxin was absorbed too slowly or in too small amounts to produce a general skin reaction. In such cases one would expect a change in skin sensitivity and immunity similar to that artificially produced by injections of toxin. In this connection, it is of interest that there was a definite decrease in the percentage of sensitive children who were more than 6 years of age. With the more numerous contacts of children in the school age, an increased exposure to infection occurs, and it may be that an increase in strepto-

9. Zingher, A.: The Dick Test in Normal Persons and in Acute and Convalescent Cases of Scarlet Fever, J. A. M. A. **83**:432 (Aug. 9) 1924.

coccus infections is associated with the type of slowly developing skin immunity suggested.

SUMMARY

Skin sensitivity to scarlatinal streptococcus filtrate toxin, which was present in only a small number of infants at birth, increased slowly during the first six months and more rapidly during the last half of the first year. It remained high from the second to the sixth year and fell during the school age. Skin tests made with varying amounts of toxin showed similar variations according to the age of the subject. In the first half year, the skin of a large percentage of infants was not sensitive to large amounts (50 STD) of toxin, and that of many others insensitive to small doses was positive only to large amounts (50 STD). In many of the infants tested, demonstrable antitoxin was not present in the blood. Such infants, with little if any skin sensitivity and without antitoxin, could be found up to the end of the second year. Antitoxin was constantly demonstrable, however, in practically all children more than 2 years of age and in adults not sensitive to small amounts of toxin. The only exceptions noted were in a few persons who were not sensitive to 2 STD of toxin but who were sensitive to a slightly larger amount, and in whom antitoxin was not demonstrated by the method used. In a few instances, small amounts of antitoxin were present in persons whose skins were sensitive to small doses of toxin.

SCARLET FEVER

III. MODIFICATION OF SKIN SENSITIVITY TO TOXIN AS A RESULT OF NONSCARLATINAL INFECTIONS *

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ST. LOUIS

In the course of a study [1] of skin sensitivity to scarlatinal streptococcus filtrate toxin in infants and younger children, it was noted that those in close contact with one another in an asylum showed striking differences from children in isolated homes. These differences, together with their relation to the presence of hemolytic streptococci in the pharynx, and to the presence of antitoxin in the blood, form the subject of this report. In addition, the variation in skin sensitivity which accompanies measles and possibly some other nonscarlatinal infections has been studied.

METHOD

The skin tests were made as previously described,[1] with 2, 20 and 50 standard skin test doses (STD) of a potent scarlatinal streptococcus filtrate that contained 100,000 STD per cubic centimeter. Antitoxin determinations were made by toxin neutralization tests. Pharyngeal cultures for hemolytic streptococci were made by rubbing a sterile swab, moistened with salt solution, on the tonsils and posterior pharyngeal wall. A small amount of this material was then seeded thinly over the surface of a 100 mm. rabbit-blood agar plate. After twenty-four hours of incubation, the hemolytic streptococcus colonies were counted, and smears were made of fished colonies to verify the morphology. In selected cases, the organisms were isolated and tested for neutralizable toxin. For these tests a filtrate from 5 day veal infusion broth culture with an original p_H of 7.8 was used. The addition of 0.1 per cent of dextrose and heating the mixture until a fairly deep brown color appeared (one hour at 20 pounds [9 Kg.] steam pressure) seemed to facilitate the production of toxin. Each filtrate was tested in 0.1 cc. amounts of 1:100, 1:250 and 1:500 dilutions, on four children known to be positive to 1 STD, and on four others known to be negative to 50 STD of scarlatinal filtrate toxin. In those filtrates to which the children gave positive reactions, neutralization tests were made with convalescent scarlet fever serum which showed neutralizing antitoxin in dilutions of 1:100. All of the children gave negative reactions to the filtrates heated for two hours at 100 C.

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* From the Department of Pediatrics, Washington University School of Medicine and the St. Louis Children's Hospital.

1. Cooke, J. V.: Scarlet Fever: I. The Relation Between Antitoxin in the Blood and Skin Sensitivity to Toxin in New-Born Infants and Their Mothers, Am. J. Dis. Child. **34**:969 (Dec.) 1927; Scarlet Fever: II. The Development of Toxin Sensitivity of the Skin in Infants and Its Relation to the Presence of Antitoxin in the Blood, ibid., this issue, p. 762.

Infants and children from the St. Anne's asylum, a foundling home, formed the group of institutional children who were examined. The study was made possible through the kindness of Dr. Jules M. Brady and the Sisters in charge. Here, after leaving the nursery, the children are kept in three large wards: (*a*) those from 3 months to 1 year of age, (*b*) those from 1 to 2 years, and (*c*) those from 2 to 6 years of age. In these wards, the younger infants, under normal conditions, are not isolated, and the runabouts are in intimate contact with one another, so that there is constantly an opportunity for dissemination of infections of the upper respiratory tract. Rhinitis, pharyngitis and otitis are not infrequent and tend to spread in a ward when started. At times, small epidemics of chickenpox, whooping cough and measles have occurred, but, with the exception of one case to be mentioned subsequently, scarlet fever has not occurred among these children. They are, as a group, well nourished and active. At the time of these examinations (April-May), there was a moderate and apparently usual amount of subacute

TABLE 1.—*Skin Sensitivity to Scarlatinal Toxin in One Hundred and Eight Young Children in a Foundling Home*

Age	Number	Skin Reactions			
		+2 STD	+20 STD	+50 STD	−50 STD
2 to 6 months	22	5	7	4	6
6 to 12 months	26	1	9	9	7
1 to 2 years	20	3	13	3	1
2 to 3 years	19	0	8	5	6
3 to 6 years	21	0	6	3	12

rhinitis and a few cases of chronic otitis media, but none of the children was considered ill.

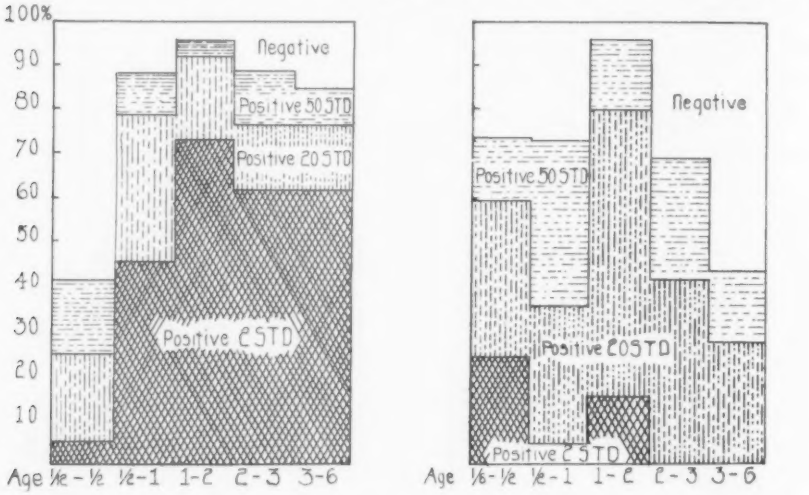
The relation of clinical scarlet fever to this foundling home is interesting. For a number of years, a case of this disease had not occurred until a few weeks previous to the time of the tests here recorded. At this time, a child, aged 4, from outside the home, was admitted to the older children's ward (ward *c*). She developed typical scarlet fever six days later. The disease did not occur in any other child.

The control children from more isolated homes consisted of an unselected group from one of the municipal health clinics and were examined through the kindness of Dr. Hugh McCulloch. They were from families of the working class, such as artisans and clerks, living under good hygienic conditions, and they were free from any demonstrable infection. They were examined at approximately the same time of the year as the children in the institutional group.

The relative skin sensitivity to varying amounts of scarlatinal filtrate toxin in 108 children from the foundling home, with the number tested

in different age groups, is shown in table 1. In order to make apparent the differences between these children and noninstitutional children, the percentage of positive reactions in the two classes is shown graphically in chart 1. For the normal controls, the results in 575 children previously reported [2] have been tabulated in the same age groups. It is apparent that with the relatively small numbers in the institutional group, percentage comparisons are subject to error, but the differences are so extreme that they cannot be attributed to the selection inherent in small groups.

In the chart the marked lowering of skin sensitivity in the institutional children between 6 months and 6 years is evident, although there is a greater sensitivity in those less than 6 months of age. The fact that the skin of not one of forty children over 2 years of age was



Comparison of relative skin sensitivity to scarlatinal toxin in children from isolated homes and from an institution. The figure on the left shows the results for the normal control subjects; that on the right, those for the institutional children.

sensitive to 2 STD of toxin and that the skin reactions of almost half of those in this ward were negative to as much as 50 STD of toxin is especially striking when compared to the normal control curve.

Since it was of interest to know whether or not this relative lack of skin sensitivity was accompanied by the presence of antitoxin in the blood, five of these children, between 9 and 12 months of age, with negative reactions to 50 STD of toxin, were tested by serum neutralization tests. In all five, antitoxin was found in the blood. This indicates that the lack of skin sensitivity to toxin is probably dependent on

2. Cooke (footnote 1, second reference).

specific antibody in the blood, and is consequently an immunity rather than a lack of skin reactivity.

Such marked immunity of the skin to streptococcus filtrate toxin warranted a suspicion that the children in this institution might have acquired it from hemolytic streptococcus infections, and cultures from the pharynx were, therefore, made on 100 of these children, a few of those under 3 months of age being omitted. The cultures were taken as previously described, and the number of hemolytic streptococcus colonies counted. In table 2 the results of this examination are recorded. It will be seen that in almost two thirds of the children examined, hemolytic streptococci were demonstrable; in almost half, more than a few colonies were found, and in one-fifth, large numbers were found. The distribution was apparently less widespread in the younger infants.

As a control group, cultures were also taken from 100 children previously referred to from the municipal health clinic. Thirty-eight were between 4 and 12 months of age, thirty-five in the second year and

TABLE 2.—*Distribution of Hemolytic Streptococci in Young Children in a Foundling Home*

Age	Number	Colonies of Hemolytic Streptococci			
		None	1 to 10	11 to 50	More than 50
Ward A, 3 to 12 months	40	23	5	9	3
Ward B, 1 to 2 years	20	3	10	3	4
Ward C, 2 to 6 years	40	10	5	12	13
Totals	100	36	20	24	20

twenty-seven between the ages of 2 and 6 years. Cultures taken by the same technic showed only one in which hemolytic streptococci were present, and in this they were numerous. This was from a child, aged 2 years, who was apparently healthy. In a large number of the cultures from the throat taken in both groups, nonhemolytic streptococci, usually giving greenish colonies, were present among other organisms. None of a considerable group of these, which were subplanted, showed hemolysis. The low incidence of hemolytic streptococci found in the control group was unexpected, and can be accounted for only by the fact that these children represent a selected group in which there is close medical supervision of general health, intelligent parental care and relative isolation from sources of infection. The skin sensitivity to toxin in the control group did not show an apparent difference from that in the larger normal group shown in chart 1, and has not been separately tabulated. Indeed, almost 200 children from the same health center are included in the larger group.

Of the strains of hemolytic streptococci isolated from the institutional children, twelve chosen at random were tested for the production of

toxin by the method previously described.[2] The results of these tests, together with those of the single strain found in the control group, are shown in table 3.

It will be seen from table 3 that six of the strains gave filtrates with which a skin reaction was not obtained with 0.1 cc. of a 1 : 100 dilution. Filtrates from two other strains gave positive tests in 1 : 100 dilution but reacted with all children tested, even those who were immune to the standard scarlatinal streptococcus filtrate. This skin reactive substance was not neutralized by serum containing antitoxin. Of the remaining five strains, four gave filtrates which reacted in 1 : 500 dilution and one which gave positive tests in 1 : 250 solution. These reactions were obtained only in children whose skin was sensitive to the scarlatinal toxin. All five of these filtrates were neutralized by convalescent scarlet fever serum.

TABLE 3.—*Production of Toxin by Hemolytic Streptococci Isolated from Apparently Normal Children*

Name	Age	Skin Test	Hemolytic Streptococcus Colonies	Filtrate Reactions			
				Dick + Children	Dick — Children	Dilution	Neutralization
Herbert	4½ months	+ 20 STD	50+	—	—	1:100	
Matthew	9 months	—	45	+	+	1:100	—
Leo	9 months	—	30	+	—	1:500	+
John	9½ months	+ 50 STD	50+	+	—	1:500	+
Tommy	13 months	+ 20 STD	50+	—	—	1:100	
Agatha	14 months	+ 50 STD	50+	—	—	1:100	
George	23 months	+ 2 STD	8	+	+	1:100	—
Jane	2½ years	—	19	+	—	1:500	+
Eugene	3 years	—	50+	—	—	1:100	
Jack	4 years	—	50+	—	—	1:100	
Norma	4 years	—	50+	+	—	1:500	+
Blanche	5 years	—	50+	+	—	1:250	+
Edward*	2 years	+ 20 STD	50+	—	—	1:100	

* This child was not from the institution.

In five children from the foundling home, therefore, pharyngeal cultures showed hemolytic streptococci, filtrates from which could not be distinguished by skin tests from similar streptococci of scarlatinal origin, and which were neutralized by convalescent scarlet fever serum. In the other strains, the neutralizable skin reactive substance was not demonstrated.

MEASLES

One infection which seems definitely to affect the skin sensitivity to scarlatinal toxin is measles. It is stated by Paraf [3] that while a number of patients with uncomplicated measles had positive reactions to the Dick test, during both the eruptive stage and later, others with complications had positive reactions at first which became negative later. This

3. Paraf, J.: La réaction de Dick an cours de la rougeole, Bull. et mém. Soc. méd. d. hôp. de Paris **50**:506 (March 19) 1926.

he attributes to an immunity from a complicating streptococcus infection. Kleinschmidt [4] found a large number of children with measles in whom the reaction to the Dick test was negative during the stage of eruption and positive afterward. Gorter, De Korte and Munk [5] also have reported that the reaction to the Dick test was constantly modified during the course of measles, becoming negative during the period of eruption and positive again after recovery. They noted, too, that the serum of a child whose reaction to the Dick test had become negative during measles did not neutralize toxin—an observation at variance with that from other children with a negative reaction to the Dick test who did not have measles.

By making skin tests with varying amounts (2, 20 and 50 STD) of toxin at intervals, the relative skin reactivity before, during, and after measles has been determined during an epidemic in a small ward. The number of cases available was small, but the quantitative changes noted

TABLE 4.—*Skin Sensitivity to Scarlatinal Toxin During and After Measles*

		Skin Reaction to Toxin Before and During Successive Weeks After Onset of Measles *								
Case No.	Age in Years	Before	1	2	3	4	5	6	7	Complications
R. S. 1	6	+	—	—	+	+	++	..	..	Otitis media, 2d week
B. C. 2	6	—	—	—	+	+	++	++	++	None
R. F. 3	7	+++	—	—	++	+++	++	+++	+++	Rhinopharyngitis, acute, 3d week
M. M. 4	7	++	++	++	++	++	+++	+++	+++	None
M. H. 5	7	+++	++	++	+++	+++	.....	.....	.....	Rhinopharyngitis, acute, 3d week
G. H. 6	8	++	—	—	+	++	++	+++	++	Otitis media, 2d week
K. W. 7	9	++	—	—	—	—	—	+	+	Bronchitis, acute, 2d week
C. H. 8	9	+++	+++	+++	+++	+++	..	..	..	None
T. G. 9	14	..	..	—	—	..	..	..	..	None

* In this table, +++ indicates a positive reaction to 2 STD; ++, positive to 20 STD; +, positive to 50 STD, and —, negative to 50 STD.

appear definite. They are shown in table 4. In this table, the degree of skin sensitivity to the toxin during the various weeks is indicated by +++, ++, + and —, depending on whether 2, 20 or 50 STD was required to cause a positive skin reaction or whether a reaction did not occur with 50 STD. It will be seen that in the majority of the cases the skin sensitivity to toxin was decreased during the acute stage of the disease, as compared with the periods before the onset and after the second week of convalescence. In a few, little if any change was noted. The greatest change appeared in case 3, in which positive skin reactions were given by 2 STD before the onset of measles, while during the acute phase of the disease a skin reaction was not obtained with 50 STD,

4. Kleinschmidt, H.: Ueber die Dicksche Reaktion, Klin. Wchnschr. **4**:234 (Dec. 3) 1925.

5. Gorter, E.; De Korte, M., and Munk, J.: Recherches sur la scarlatine, Acta Paediat. **6**:383 (May 28) 1927.

and later the skin sensitivity returned. In this case the blood had been tested for antitoxin previous to the attack of measles. It was tested again during the first week of the disease, when the skin did not react with 50 STD of the toxin. Antitoxin was not found at either time. All the complications listed were mild, and in no instance with complications was there a late decrease in skin sensitivity. In general, this group of cases shows a definite decrease in skin sensitivity during the eruptive stage of measles and corresponds with the changes described by Kleinschmidt and by Gorter.

In considering the possible explanation for this loss of skin sensitivity to scarlatinal streptococcus filtrate toxin in measles, the variations in skin reactivity to other substances during this infection are of interest. The well known decrease in skin sensitiveness to tuberculin during measles, first described by Preisich [6] and Pirquet,[7] has been confirmed repeatedly, although with the use of intradermal injections Grüner [8] has shown that this lack of cutaneous reaction is relative and not always absolute. The cutaneous hypersensitivity to horse serum has likewise been shown to disappear during measles (Hamburger,[9] Bessau [10]).

On the other hand, skin reactions to primarily toxic substances such as diphtheria toxin are not influenced by measles (Bessau,[10] Zingher,[11] Lereboullet,[12] Renault and Levy [13]), and it has been found that no change in the antitoxin content of the blood occurs during the measles exanthem (Karasawa and Schick [14]). The loss of skin sensitivity in

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6. Preisich: Budapester Ärzteverein, Nov. 9, 1907, quoted by Pirquet (footnote 7).

7. Pirquet, C.: Das Verhalten der kutanen Tuberkulinreaktion während der Masern, Deutsche med. Wchnschr. **34**:1297 (July 23) 1908.

8. Grüner, O.: Ueber die Herabsetzung der Tuberkulinempfindlichkeit Tuberkulöser nährend der Masern, München. med. Wchnschr. **56**:1681 (Aug. 17) 1909.

9. Hamburger, F.: Ueber Allergieabnahme während der Masern und über gegenseitige Beeinflussung zweier Infektionskrankheiten, München. med. Wchnschr. **57**:1203 (May 31) 1910.

10. Bessau, G.; Schwenke, J., and Pringsheim, J.: Ueber die Masernantianaphylaxie, Jahrb. f. Kinderh. **81**:293, 1915.

11. Zingher, A.: The Schick Test in Poliomyelitis, Scarlet Fever, Measles and in Normal Children, Am. J. Dis. Child. **13**:247 (March) 1917.

12. Lereboullet, P.; Marie, P. L., and Brizard: La réaction de Schick, dans la rougeole, Bull. et mém. Soc. méd. d. hôp. de Paris **45**:1210 (July 29) 1921.

13. Renault, J., and Levy, P. P.: Pathogénie de la diphtérie secondaire et diphtérino-reaction de Schick; Absence d' anergie à la diphtérie dans la rougeole, Bull. et mém. Soc. méd. d. hôp. de Paris **44**:816, 1920.

14. Karasawa, M., and Schick, B.: Ueber den Gehalt des Serums diphtherie- und masernkranker Kinder an Schutzkörper gegen Diphtherie-toxin, Jahrb. f. Kinderh. **72**:460, 1910.

measles is apparently limited to those substances (antigens) to which the individual is hypersensitive in an anaphylactic sense, since the skin reactivity to primarily toxic substances is unaffected. The condition has been generally regarded as "anergie" or lack of reactivity, and is sometimes referred to as antianaphylaxis. The skin sensitivity to scarlatinal streptococcus filtrate protein (toxin) is temporarily decreased or lost during an attack of measles in a manner apparently identical with the "anergie" to protein antigens. This supports the view that the effect of the filtrate toxin is dependent on a specific skin hypersensitivity rather than a true exotoxin action.

In certain other acute infections it has been noted that a similar decrease in skin hypersensitivity occurs at times, but such nonspecific desensitization is apparently much less frequent than in measles. The skin sensitivity to scarlatinal toxin also is occasionally decreased during such infections as pneumonia, but many cases of various types of acute infections have been observed in which the skin sensitivity was unchanged.

OTHER OBSERVATIONS

In a considerable number of instances, the skin sensitivity of apparently normal older children has been tested at intervals of from a few months to a year or more. Although most of these tests did not show any differences, in others a considerable difference was noted between the first test and later ones. Not only did a marked sensitivity decrease or disappear, but children with an apparent absence of sensitivity to a considerable amount (50 STD) of toxin were later shown to react regularly to small amounts (2 STD). None of these children had had scarlet fever in the interval between tests, but, of course, may have suffered from other types of minor infections of the upper respiratory tract.

A phenomenon which has been of special interest is the alteration in sensitivity of children with a positive reaction to the Dick test following repeated intradermal injections of toxin. In a number of such children in whom repeated intracutaneous injections were made, a change in skin sensitivity did not occur. In others, however, two types of changes in skin reactivity were noted. In one group, after such repeated tests, the children gave negative skin reactions sometimes even to considerable amounts (50 STD) of toxin, and those so tested showed neutralizing antibody in the blood. In the second group the subjects continued to give positive skin tests to small amounts of toxin alone and no reaction with heated filtrate. When neutralization tests were made in such children, however, nonblanching, antitoxin-free serums, which had previously failed to neutralize toxin in the same children, and which still failed to do so in other children, now were found to inhibit the toxin

when the mixture was tested. In several children of this second type tested, neutralizing antitoxin could not be demonstrated in the blood. Such reactions have also been noted in children who had not previously had a number of intracutaneous injections of toxin. Because of this unexplained type of skin reactivity, the necessity for preliminary tests and the employment of several children and controls in each toxin neutralization test for antitoxin is apparent. It is possible, for example, to have persons whose skin is apparently sensitive to toxin, but who are not suitable for testing for antitoxin by toxin neutralization.

SUMMARY

In a study of more than 100 apparently well younger children not isolated from one another in a foundling home, the following observations were made:

1. The skin sensitivity to scarlatinal streptococcus filtrate toxin was greatly decreased in this group when compared to healthy children of the same ages from isolated homes.

2. In a few of the children so tested the decreased skin sensitivity was apparently due to the immunity accompanying circulating antitoxin.

3. The incidence of hemolytic streptococci in cultures from the pharynx of the children in the institutional group was much greater than in a control group from isolated homes.

4. In the study of filtrates from the strains of hemolytic streptococci isolated from the pharynx, the skin reactive substance apparently identical with scarlatinal toxin was demonstrated in some of the strains, but not in all. It was neutralizable by convalescent scarlet fever serum containing antitoxin.

During an epidemic of measles in a small ward, a marked diminution in skin sensitivity to scarlatinal streptococcus filtrate toxin occurred during the acute phase of the infection. During convalescence this skin sensitivity returned. It was suggested that during an attack of measles the "anergie" or lack of skin reactivity which occurs to such antigens as tuberculin and horse serum includes also the antigenic fraction of scarlatinal streptococcus filtrates.

Certain observed changes in skin sensitivity to scarlatinal streptococcus filtrate in children tested at intervals were mentioned as possibly due to non-scarlatinal infections or to a decrease in circulating antibody. Alterations in skin reactivity which have followed intracutaneous injections of the scarlatinal filtrate toxin were described.

SCARLET FEVER

IV. TOXIN PRODUCTION BY HEMOLYTIC STREPTOCOCCI FROM NONSCARLATINAL INFECTIONS IN INFANTS *

JEAN V. COOKE, M.D

WITH THE TECHNICAL ASSISTANCE OF NELLIE BRINKERHOFF

ST. LOUIS

A previous study [1] of hemolytic streptococci isolated from pharyngeal cultures of apparently healthy infants and young children showed that certain strains produced a skin reactive substance which was neutralized by convalescent scarlet fever serum. This was apparently identical with that formed by strains of hemolytic streptococci of scarlatinal origin. A similar study of organisms recovered from acute infections of the ear and mastoid in sick infants has been made.

The organisms were isolated on rabbit blood agar from patients under 2 years of age in the St. Louis Children's Hospital. All cultures were obtained from swabs which had received purulent material from the paracentesis knife just after myringotomy for acute otitis media, or that taken from the mastoid antrum at operation. In order to illustrate the relative prevalence of hemolytic streptococci in such infections of infants, 100 consecutive cultures from different infants have been tabulated in table 1. These do not include all infants in the hospital suffering from acute infections of the ear and mastoid, but only those from whom material was sent to the laboratory for bacteriologic diagnosis.

The organisms noted in table 1 were usually in relatively pure culture, and gave an abundant growth. In the tabulation, the only feature especially noteworthy is the rather large proportion of cases in which hemolytic streptococci were the etiologic factor. This is particularly true of infections involving the mastoid. While figures are not available for infants with similar infections of the upper respiratory tract, which were not sufficiently severe to require operative measures, it seems likely that in these also hemolytic streptococci occur frequently.

In fourteen of the infections tabulated, the hemolytic streptococci isolated were grown on blood-free broth, and the filtrate was tested for toxin by the same technic used in the series previously studied.[1] Each filtrate was tested on at least four children who were sensitive to 1 skin test dose (STD) of standard scarlatinal toxin, and on four others who

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* From the Department of Pediatrics, Washington University School of Medicine and the St. Louis Children's Hospital.

1. Cooke, J. V.: Scarlet Fever: III. Modification of Skin Sensitivity to Toxin as a Result of Nonscarlatinal Infections, Am. J. Dis. Child., this issue, p. 772.

were not sensitive to 50 STD of the same standard toxin. Dilutions of 1:250 and 1:500 were used intradermally in 0.1 cc. amounts with controls of the 1:250 dilution heated to 100 C. for two hours. If skin reactions occurred, neutralization tests were made with undiluted convalescent scarlet fever serum which neutralized the standard scarlatinal toxin in a dilution of 1:100, and control neutralization tests with normal human serum shown to be free from neutralizing antibody for the standard toxin.

TABLE 1.—*Micro-organisms Isolated from 100 Cases of Acute Otitis Media and Acute Infections of the Mastoid Antrum in Infants*

Source	Number	Hemolytic Streptococcus	Nonhemolytic Streptococcus	Staphylococcus aureus	Pneumococcus	Bacillus pyocyaneus	Diphtheroid bacilli	Bacillus coli	Micrococcus tetragenus	No Growth
Ear	32	7	2	15	1	0	4	0	2	1
Mastoid Antrum	68	42	1	7	3	3	1	1	2	8
Totals	100	49	3	22	4	3	5	1	4	9

TABLE 2.—*Filtrate Toxin Production by Hemolytic Streptococci from Nonscarlatinal Mastoid Infections in Young Infants*

		Dick + Children		Dick — Children		Neutralization	
Age	Source	Reaction	Dilution	Reaction	Dilution	Convalescent Scarlet Fever Serum	Normal Serum
6 wks.	Mastoid	+	1:500	—	1:250	+	—
2 mos.	Mastoid	+	1:500	—	1:250	+	—
3 mos.	Blood	+	1:500	—	1:100	+	—
4 mos.	Blood	+	1:500	—	1:250	+	—
7 mos.	Mastoid	+	1:10000	—	1:250	+	—
9 mos.	Mastoid	+	1:250	—	1:100	+	—
10 mos.	Mastoid	+	1:500	—	1:100	+	—
11 mos.	Mastoid	+	1:500	—	1:100	+	—

In general, the filtrates fell into two groups: (1) those which regularly gave positive skin reactions in the sensitive children, negative reactions in the nonsensitive children and were neutralized by normal antitoxin-free human serum, and (2) those which reacted irregularly and did not conform to the reactions of the first group.

In table 2 are shown the results of filtrate tests on eight strains of hemolytic streptococci which reacted regularly and in which the filtrates appeared indistinguishable from those of similar organisms of scarlatinal origin. It will be noted that most of the filtrates gave positive skin reactions in dilutions of 1:500. They were not regularly tested in higher dilutions, but the size and character of these skin reactions indicated that if a higher dilution was used, the reaction would be negative. In only one filtrate was there formed a potent toxin which gave positive

reactions in 1 : 10,000 dilutions. It is of some interest that in this case strains from both the right and left mastoid antrums gave similarly potent filtrates. None of the filtrates tabulated gave positive reactions after heating for two hours at 100 C.

Tests of the skin sensitivity to scarlatinal filtrate toxin of the infants from whom the strains of hemolytic streptococci were isolated had been made in six of the eight cases before or at the early onset of the infection. In two (2 months and 4 months), the skin reactions were negative to 50 STD, and no neutralizing antitoxin was found in the blood. Two other infants (7 months and 11 months) gave negative reactions with 2 STD but positive reactions with 20 STD. In neither of these could neutralizing antibody be demonstrated. The remaining two infants (9 months and 10 months) had given positive reactions to 2 STD of toxin, but in both a transfusion of blood was made just before the mastoid operation, and later reactions were negative to 2 STD but positive to 20 STD in both infants.

Filtrates of six other strains of hemolytic streptococci similarly isolated from mastoid infections in infants less than 1 year of age gave more irregular results. In one, positive skin reactions were not obtained even when a dilution of 1 : 100 was used. The remaining five gave positive reactions in dilutions of 1 : 100 to 1 : 500 not only in children sensitive to the standard scarlatinal filtrate, but also in some nonsensitive children. In two instances, the filtrate was neutralized by the normal antitoxin-free serum and not by the convalescent scarlatinal serum; in two others, both serums neutralized the skin reactive substance of the filtrates.

It would appear that specific neutralizable skin reactive substances of the type usually found in filtrates of hemolytic streptococci of scarlatinal origin can be demonstrated in many strains from infections of the upper respiratory tract in young infants; in other strains, skin reactive substances present in the filtrate do not exhibit the same apparent specificity.

SUMMARY

Hemolytic streptococci were found to be relatively frequent as a cause of infections of the upper respiratory tract in infants, especially of those which involved the ear and mastoid. Culture filtrates from many of these strains gave skin reactions which were apparently identical with those of filtrates from strains of hemolytic streptococci of scarlatinal origin, and which were neutralizable only by serums capable of neutralizing scarlatinal toxin. In filtrates from other strains, the skin reactive substance was not similarly specific and neutralizable.

SCARLET FEVER

V. THE CHANGES IN SKIN SENSITIVITY TO SCARLATINAL STREPTOCOCCUS FILTRATE IN CHILDREN FOLLOWING THE INTRODUCTION OF HOMOLOGOUS SERUMS*

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In two previous papers,[1] evidence has been presented to show that the skin of new-born infants is not sensitive to scarlatinal streptococcus filtrate toxin except in relatively few instances, and that the absence of this skin sensitivity is not due entirely to the presence of antitoxin. It was shown also that the skin of almost all infants more than 6 months of age has become sensitive to the toxin, although in some the sensitivity is more marked than in others. In a relatively small number, the skin does not show any reaction to considerable amounts of toxin. Some of these nonreactors have antitoxin in the blood, which presumably affects the sensitivity of the skin, while in the others antitoxin is not demonstrable. It was suggested[2] that the skin sensitivity might be evidence of a specific hypersusceptibility of the body cells to protein substances formed by the scarlatinal streptococcus.

A natural outgrowth of this hypothesis is the possibility of the artificial production of sensitivity in nonsensitive persons. It has not been possible to study the effect of injections of small amounts of toxin on the sensitivity of the skin of such nonsensitive persons in an attempt to cause active sensitization. This was difficult because of the relatively small number of nonsensitive persons without immunity except in early infancy, and also because these subjects could not be kept under observation for a sufficiently long period. It was possible, however, to attempt the passive transfer of skin sensitivity in certain cases. In the present paper are reported the changes in skin sensitivity which followed the injection of serum from sensitive to nonsensitive or only slightly sensitive persons.

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* From the Department of Pediatrics, Washington University School of Medicine and the St. Louis Children's Hospital.

1. Cooke, J. V.: Scarlet Fever: I. The Relation Between Antitoxin in the Blood and Skin Sensitivity to Toxin in New-born Infants and their Mothers, Am. J. Dis. Child. **34**:969 (Dec.) 1927; Scarlet Fever: II. The Development of Toxin Sensitivity of the Skin in Infants and Its Relation to the Presence of Antitoxin in the Blood, ibid., this issue, p. 762.

2. Cooke (footnote 1, second reference).

The methods used in making the skin tests and antitoxin determinations have been previously described.[1] The largest intradermal injection of filtrate given was 50 standard skin test doses (STD) of toxin, representing 0.0005 cc. of the filtrate.

EXPERIMENTAL WORK

In the first experiments, the effect of giving the subject blood from another person whose skin was sensitive to a small amount of toxin was observed. These are detailed subsequently.

Experiment 1.—W. L., a girl, aged 6 months, breast fed, with congenital malformation of the ureter and pyuria, had had a suprapubic cystostomy and a direct transfusion of 100 cc. of blood from her mother a month previous to observation. The urine from the infected bladder contained *Bacillus coli* and pneumococcus. The first tests, made when the infant was in fairly good condition and weighed 4,800 Gm., showed that the skin was slightly sensitive to toxin, giving a positive reaction 10 mm. in diameter to 50 STD, but a negative

TABLE 1.—*Skin Tests to Varying Amounts of Toxin with Measurements in Millimeters*

Date	2 STD	20 STD	50 STD
11/ 1	—	—	+ (10 × 10)
11/ 3	Transfusion, 90 cc.		
11/ 6	+ (10 × 10)*	+ (10 × 10)	+ (10 × 15)
11/10	+ (10 × 10)	+ (12 × 15)	+ (15 × 15)
11/15	—	+ (7 × 10)	+ (10 × 15)
11/19	—	+ (5 × 10)*	+ (8 × 10)
11/22	—	+ (5 × 10)	+ (13 × 13)

* Very faint or "ghost" type of erythema.

one to 20 STD. Antitoxin was not found in the blood. A transfusion of 90 cc. was given from the mother, whose skin reaction was positive to 2 STD and whose blood did not contain antitoxin. The results of skin tests made at intervals later are shown in table 1.

On the date of the last test, a specimen of blood did not show any antitoxin. At this time, the infant developed a bilateral acute otitis media due to nonhemolytic green streptococci, with mastoid involvement later and death. During the four weeks of this intercurrent infection, the general condition was poor, necessitating daily injections of dextrose or Ringer's solution. Another transfusion from the same donor during this time was followed by a larger and more intense skin reaction to 50 and to 20 STD, although when a smaller amount of toxin (2 STD) was used, the reactions remained negative. The condition of the patient during the tests after the second transfusion was such that conclusions do not seem justifiable from the apparent intensification of the skin reactions.

The opportunity for the foregoing experiment was somewhat fortuitous, since the patient required transfusion and the donor was of the desired type. In the second experiment, homologous serum was given intramuscularly to a baby after preliminary tests had been made.

Experiment 2.—L. R., a breast-fed infant, aged 9 months, and weighing 6,700 Gm., with bilateral chronic otitis media of a month's duration, without fever

and not acutely ill, had a bilateral mastoid antrotomy for postauricular drainage. Cultures from each antrum showed type IV pneumococcus. Skin reactions were negative to 2, 20 and 50 STD of toxin. The serum did not show antitoxin by neutralization tests, and 0.5 cc. did not blanch an acute scarlet fever rash. The mother's skin reaction was positive to 2 STD. The sensitizing serum, which did not contain antitoxin either by toxin neutralization tests or by a blanching test with 0.5 cc., was obtained from a boy, aged 12, who gave a positive skin reaction to 0.25 STD of toxin. The results of skin tests made before and after the intramuscular injection of 15 cc. of serum are given in table 2.

During the time these skin tests were made, the infant was in good general condition and was gaining in weight, although the surgical (mastoid) wound healed rather slowly.

In both these experiments, there was a definite and marked increase in the sensitivity of the skin following the administration of serum. In both, the development of the sensitiveness was gradual, as indicated

TABLE 2.—*Skin Reactions to Varying Amounts of Toxin, with Measurements in Millimeters*

Date	2 STD	20 STD	50 STD
1/20	—	—	—
1/24	—	—	—
1/28	15 cc. serum, intramuscularly		
1/31	—	± (7 × 7)	+ (13 × 13)
2/ 3	+ (10 × 10)*	+ (10 × 15)	+ (15 × 15)
2/ 7	+ (15 × 15)	+ (15 × 15)	+ (20 × 20)
2/10	—	± (5 × 5)	+ (15 × 20)*
2/14	+ (10 × 10)*	+ (10 × 15)	+ (15 × 15)
2/17	+ (10 × 10)*	+ (15 × 15)*	+ (20 × 20)*
2/24	+ (10 × 10)	+ (10 × 15)	+ (15 × 15)
2/28	—	+ (10 × 10)	+ (10 × 15)
3/ 4	+ (10 × 10)	+ (10 × 10)	+ (15 × 15)
3/ 9	+ (10 × 10)	+ (10 × 10)	+ (15 × 15)

* A faint "ghost" reaction appeared in these instances.

by the increasing intensity of the reactions and by the reaction to smaller amounts of the antigen. In the first case, the maximum skin reactions occurred on the seventh day and then became weaker. In the second case, the most intense reactions occurred on the ninth day, and the sensitiveness persisted for at least a month, although later the reactions became slightly less well marked to small amounts of toxin. Children with negative reactions to 20 STD or more of toxin and without neutralizing antibody in the blood have been infrequently recognized, at least after the period of early infancy, and in only one other of this type has a similar experiment been tried. This child, an infant 6 months of age, did not show skin sensitivity to 50 STD or less of toxin either before or for eight days after the injection of 12 cc. of serum from a child with a positive reaction to the Dick test. In children whose skin is sensitive to as little as 20 STD of toxin, any marked increase in sensitivity would seem more difficult to demonstrate with certainty, so that less sensitive subjects only were used.

Although it has not been possible to enlarge the series by including other children with neither skin sensitivity nor immunity, others without

skin sensitivity but with demonstrable neutralizing antibody in the blood have been tested following injections of homologous serum.

The second series consisted of eight infants of this type in the latter part of the first year from an orphanage in which a study [3] was made. From only five of these infants could blood be obtained, but in all there was evidence of neutralizing antitoxin, although the tests indicated that it was not present in large amounts. Each was given intramuscularly 10 cc. of serum from a child who gave a positive skin reaction when less than 1 STD of toxin was used. Three of these showed definite although transient increases in skin sensitivity following the introduction of the serum. The results of these tests are shown in table 3.

TABLE 3.—*Changes in Skin Sensitivity Following Injection of Homologous Serum*

		Skin Reaction to Varying Amount of Toxin and Measurements in Millimeters								
		Lawrence, 8½ mo.			Robert, 10½ mo.			Matthew, 9 mo.		
Date		2 STD	20 STD	50 STD	2 STD	20 STD	50 STD	2 STD	20 STD	50 STD
4/11	Control	—	—	± 7×7	—	—	+ 7×10	—	—	—
4/13	Control	—	—	± 5×5	—	—	+ 7×10	—	—	—
4/18	Serum, 10 cc.									
4/21	Third day	—	± 7×7	+ 10×10	—	+ 13×13	+ 15×15	—	—	—
4/25	Seventh day	—	+ 8×10	+ 10×10	± 5×5	+ 15×15	+ 18×20	—	—	+ 10×10
4/28	Tenth day	+ 10×10	+ 10×10	+ 15×15	—	+ 10×10	+ 15×15	—	—	± 7×7
5/ 3	Fifteenth day	—	—	± 7×7	—	+ 10×10	+ 10×10	—	—	—

In two of the infants shown (Lawrence and Robert), there was some skin sensitivity to the largest amount (50 STD) before the injection of serum. In both there was a gradual increase in the sensitivity to smaller amounts (20 and 2 STD), which reached the maximum on the seventh to the tenth day after the serum was given. This increased sensitivity did not persist. The third infant (Matthew), who did not give any reaction to 50 STD in the preliminary tests, showed a transient sensitivity to this quantity on the seventh and tenth days only after the injection of serum.

Three of the remaining five children in this series who were given serum at the same time did not show any change in the skin reactivity, although in two of them a small area of redness from 3 to 4 mm. in diameter was noted at the points of injection from the seventh to the tenth day only. In the other two, hyperemic areas, from 5 to 7 mm. in diameter, developed after the same interval. Those reactions seemed

3. Cooke, J. V.: Scarlet Fever: III. Modification of Skin Sensitivity to Toxin as a Result of Nonscarlatinal Infections, Am. J. Dis. Child., this issue, p. 772.

so much less definite than those of the three tabulated that they were considered inconclusive or negative and will not be shown in detail.

In the experiments already recorded it seems evident that, under certain conditions, an induced skin sensitivity to scarlatinal streptococcus filtrate toxin may be produced, or the degree of a sensitivity already present may be increased in infants. Although circulating neutralizing antibody may have some influence on the development of sensitivity, its presence in small amounts did not prevent the appearance of transient skin sensitivity in certain cases.

Although in infants an increase in skin sensitivity followed the introduction of serum in the instances cited, such a change could not be demonstrated in older children. In a series of six children from 5 to 10 years of age, skin tests were made twice weekly during a period of three weeks. One gave a positive reaction to 20 STD, three gave positive reactions to 50 STD and two gave negative reactions to 50 STD of toxin. Reactions for neutralizing antitoxin were positive in the serum from each child. During the preliminary period of control tests, a significant change did not occur in the reactions, although occasionally there was a slight variation in size or intensity on different days to the same amount of toxin. Each child was then given intramuscularly from 15 to 18 cc. of serum from a child whose skin was sensitive to less than 1 STD of toxin. During the two following weeks, the skin reactions did not show any increase in sensitivity from that noted previous to the injection of serum.

The effect on the sensitivity of the skin of the introduction of homologous serum containing antitoxin has been noted in a certain number of instances after transfusions of blood were made. The following will serve as examples:

CASE 1.—An athreptic boy, aged 15 months, had a positive skin reaction to 20 and 50 STD of toxin, but it was negative to 2 STD. The blood did not show any antitoxin. A transfusion of 150 cc. of blood was given from the father, who gave a negative skin reaction to 50 STD and who had neutralizing antibodies in the blood. Three days later, the recipient gave a negative skin reaction to 50 STD of toxin.

CASE 2.—A boy, aged 11 months, with pneumococcus empyema gave a positive reaction to 2 STD of toxin and had no antitoxin in the blood by neutralization tests. The donor (father) had antitoxin in the blood and gave a negative skin reaction to 2 STD but a positive one to 20 and 50 STD. Three, six and eleven days after the transfusion of 130 cc. of blood, the patient gave negative skin reactions to 2 and 20 STD, but the reaction remained positive to 50 STD.

CASE 3.—A baby, aged 3 months, with harelip and cleft palate, had a negative skin reaction to 50 STD of toxin and readily demonstrable circulating antitoxin. A direct transfusion of blood was given from the mother, who also had antitoxin but a positive skin reaction to 50 STD, although a negative one to 2 and 20 STD. Seven skin tests during the month following did not show any reaction even to the larger amounts of toxin.

These instances show the usual effect of the introduction of normal serum containing neutralizing antibody on the skin sensitivity of the recipient. The skin, which may react positively to the filtrate toxin before the serum is given, shows a definitely decreased sensitivity afterward.

The skin sensitivity following local intracutaneous injections of serum from persons with a positive reaction to the Dick test has been observed in a few instances. Five older children with negative skin reactions and with antitoxin demonstrable in the blood were given intradermal injections of 0.2 cc. of nonblanching serum from a child with a positive Dick reaction. Injections of toxin into these same sites one day and three days later did not show any differences from the control tests in other areas of the skin.

COMMENT

The increase in sensitivity of the skin which followed the introduction of normal serum in certain infants as described has certain features which seem to show that the change was not an accidental observation dependent on the technic of performing the tests or on spontaneous alterations in skin sensitiveness. Of these, the most significant is the consistent and gradual increase in sensitivity to smaller amounts of the filtrate during the week following the injection of serum. It is also of interest that the changes noted occurred only in infants in whom the skin was relatively insensitive to the filtrate and in whom neutralizing antibody was not demonstrable in the blood or present only in an apparently small amount. A change was not noted following similar injections of serum into older children who had similar sensitivity of the skin but in whom antitoxin was readily demonstrable.

The production of an induced sensitivity of the skin to scarlatinal filtrate toxin by the introduction of homologous serum from a skin sensitive person seems, in certain respects, analogous to the passive transfer of hypersensitivity in anaphylactic animals. In animals, however, the anaphylactic hypersensitiveness is usually demonstrable within twenty-four hours of the injection of serum, while in sensitivity of the skin to filtrate toxin the increased sensitivity was marked only after from six to eight days. If the latter phenomenon is of an anaphylactic character, one must assume that the production of such hypersensitivity in man is accomplished much more slowly than in certain other animals. Unfortunately, there are no observations regarding the development of human anaphylactic hypersensitivity by which comparisons may be made.

SUMMARY

The skin of certain infants in the latter half of the first year was found not to be sensitive to considerable amounts of scarlatinal strepto-

coccus filtrate toxin and to have little if any neutralizing antibody in the blood. The introduction into these infants of serum from a person whose skin was sensitive to a small quantity of filtrate toxin was followed in several instances by a gradual increase in the skin sensitivity of the recipient.

In older children in whom lack of skin sensitivity was accompanied by the presence of antitoxin in the blood, an alteration in the sensitivity was not noted after the introduction of such homologous serum.

The administration of normal serum which contained neutralizing antibody was followed by a marked decrease in the sensitivity of the skin of the recipient.

The seeming analogy between this induced sensitivity in infants and a passive anaphylactic hypersensitivity was suggested.

STUDIES ON THE HEARTS OF NORMAL CHILDREN

II. ROENTGEN-RAY STUDIES *

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The clinician is interested in roentgenograms of a child's heart, largely because he hopes to determine by the size and shape of the heart whether physical conditions have pathologic significance. It would be equally important to be able to say that a heart of a given shape is definitely normal or pathologic. We have computed statistics for the normal size of the heart in children of various ages and for the normal relationships between the transverse width of the heart, height and the width of the chest. We have also attempted a classification of the shapes of normal hearts. Many studies of this kind have been made on adult hearts. The literature on the size of children's hearts is not abundant, and a considerable amount of the work was done on small groups and on children in clinics who did not have obvious organic heart disease.

This study was made over a period of seven school years and was based on yearly roentgenograms of 246 of the same group of normal school children who have been fully described in another section of this paper. All the roentgenograms were made with the child in a standing dorsoventral position, at a distance of 6 feet. The exposures varied from three-eighths to three-fourths of a second, with the central ray passing approximately through the fourth dorsal vertebra; they were made in moderately deep inspiration, except in a few cases in which the child was too young to cooperate.

Measurements of the right and left diameters of the heart and of the longitudinal diameter were taken in the standard manner.[1] The measurements of the longitudinal diameter seemed so arbitrary and bore so little relation to the actual size of the heart that the figures obtained have not been used. Bardeen [2] also found this diameter useless in obtaining a true picture of the size of the heart. Measurements of the frontal plane area according to the method of Bardeen were not made.

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* From the Bureau of Educational Experiments.
* Received for publication, Jan. 6, 1928.

1. Dietlen, H.: Herz und Gefässe im Röntgenbild, Leipzig, 1923.

2. Bardeen, C. R.: Determination of the Size of the Heart by Means of the X-Rays, Am. J. Anat. **23**:423 (March) 1918.

In spite of the difference in the physical types of these boys and girls and their marked variations in height and weight, there is a steady increase in the width of the heart as the child grows older. The sex difference also seems definite and shows that girls have smaller hearts than boys from 2 until 7 years of age. For the age period of 7 through 11, their hearts are practically equal in size, the averages varying only 0.1 cm. At the age of 12 and 13, the girls' hearts are larger than those of the boys.

TABLE 1.—*Average Transverse Width of Heart by Age and Sex, with Standard Deviations*

Age	Number of Cases	Midline to Right Border, Average	± Standard Deviations	Midline to Left Border, Average	± Standard Deviations	Transverse Diameter	± Standard Deviations
			BOYS				
2	7	2.8	0.72	5.1	0.82	7.9	0.21
3	11	2.9	0.57	5.2	0.51	8.1	0.48
4	23	2.9	0.58	5.7	0.74	8.6	0.49
5	39	2.9	0.35	5.9	0.75	8.9	0.58
6	35	3.0	0.45	6.0	0.68	9.0	0.49
7	35	3.0	0.50	6.2	0.75	9.2	0.81
8	32	3.2	0.53	6.1	0.86	9.4	0.81
9	35	3.2	0.48	6.3	0.75	9.5	0.79
10	21	3.1	0.79	6.7	0.68	9.8	0.82
11	21	3.3	0.68	6.6	0.86	9.9	0.75
12	19	3.4	0.67	6.7	0.81	10.1	0.84
13	9	3.5	0.31	6.9	0.70	10.4	0.54
			GIRLS				
2	5	3.2	0.46	4.4	0.48	7.6	0.40
3	9	3.0	0.63	5.1	0.81	8.0	0.51
4	25	2.7	0.67	5.7	0.78	8.4	0.62
5	36	2.9	0.58	5.7	0.69	8.6	0.59
6	32	2.8	0.57	6.0	0.63	8.8	0.53
7	36	2.9	0.32	6.2	0.79	9.1	0.68
8	32	3.0	0.62	6.2	0.65	9.3	0.59
9	28	3.2	0.54	6.3	0.73	9.5	0.82
10	22	3.3	0.67	6.4	0.67	9.7	0.78
11	24	3.3	0.73	6.5	0.86	9.9	0.94
12	21	3.7	0.57	6.6	0.98	10.4	0.99
13	10	3.6	0.40	7.0	1.09	10.6	0.92

RELATION OF THE RIGHT TO THE LEFT SIDE OF THE HEART

We have found that approximately one third of the heart lies to the right of the midline. This confirms Ziskin's [3] observations that the right border of the heart does not extend relatively further to the right in childhood, as had been previously supposed. Ziskin does not make any differentiation between the sexes in his tables for children from 4 to 16 years of age, but we find that while the percentage relation of the right to the left side of the heart varies only from 48 to 53 per cent in boys, in girls, the range of variation is much higher, from 42 to 57 per cent.

3. Ziskin, T.: Development and Size of the Heart in Children as Revealed by Teleoroentgen Ray Measurements, Am. J. Dis. Child. **30**:851 (Dec.) 1925.

RELATION BETWEEN THE TRANSVERSE WIDTH OF THE HEART AND THE CHEST

The transverse diameter of the heart is approximately one-half the width of the chest in normal children. Boys and girls both show this ratio (table 3). When the figures were arranged in age groups and height groups, we found that there was no evidence of a diminishing ratio with growth. Ziskin, on the contrary, found that the ratio varied from 46.3 to 40.7 per cent, the relative percentage decreasing with the growth of the child in height. De Buys and Samuel [4] did not find a constant relationship between the width of the heart and the internal diameter of the chest in a group of infants followed up from birth to the age of 39 months. In a group of thirty-nine children, Perkins [5] found the transverse width of the heart to be approximately 50 per cent of the internal diameter of the chest.

TABLE 2.—*Percentage Relation of the Right Side of the Heart to the Left Side*

Boys			Girls	
Number of Cases	Percentage Relation of Midline to Right Border to Midline to Left Border	Age	Percentage Relation of Midline to Right Border to Midline to Left Border	Number of Cases
23	52	4	45	25
39	49	5	53	36
35	51	6	48	32
35	50	7	46	36
32	53	8	49	32
35	49	9	50	27
21	48	10	51	22
21	49	11	51	24
19	52	12	57	21
9	50	13	42	10

RELATION OF THE SIZE OF THE HEART TO HEIGHT

There is a close correlation, with small standard deviations, between the transverse width of the heart and the height of the child. For boys of all ages, the transverse width of the heart varied from 7 to 8.2 per cent of the height, and in girls, the variation was 6.9 to 8.4 per cent of the height. Partial correlations were made in order to determine, if possible, which factor, height or age, is the more important in determining the size of the heart. By the product-moment method, the coefficient of correlation between the size of the heart and height is found to be $+ 0.64, \pm 0.03$, and between the size of the heart and age is found to be $+ 0.56, \pm 0.03$. The partial coefficient of correlation between the size of the heart and height with the age constant is $+ 0.38$.

4. De Buys, L. R., and Samuel, E. C.: Growth of the Heart, Am. J. Dis. Child. **30**:355 (Sept.) 1925.

5. Perkins, C. W.: Roentgen Cardiac Studies in Children, Radiology **2**:367 (June) 1924.

The partial coefficient of correlation between the size of the heart and age with the height constant is —0.05. Thus the effect of height on the size of the heart is shown to be greater than the effect of age on the size of the heart.

TABLE 3.—*Internal Diameter of the Chest by Age and Sex and Percentage Relationship of Transverse Diameter of the Heart to the Internal Diameter of the Chest*

Age	Number of Cases	Internal Diameter	± Standard Deviations	Percentage Relation of Heart to Internal Diameter	± Standard Deviations
		Boys			
2	7	15.5	0.9	49	2.0
3	11	17.2	0.6	47	3.5
4	23	17.7	0.9	48	2.5
5	38	18.6	1.0	48	3.4
6	35	19.5	1.2	47	3.9
7	35	19.7	1.3	46	3.0
8	31	20.5	1.0	46	3.5
9	33	21.1	1.2	45	3.6
10	21	21.5	1.3	46	3.3
11	19	22.0	1.1	46	2.7
12	15	23.1	1.6	43	2.7
13	9	23.6	1.2	52	8.0
		Girls			
2	5	16.4	0.5	45	2.0
3	7	16.7	1.2	47	3.2
4	24	17.6	0.8	49	2.5
5	36	17.9	0.9	48	2.7
6	32	18.4	1.2	48	3.3
7	35	19.3	1.1	47	3.1
8	30	20.0	1.2	47	3.2
9	27	20.6	1.2	46	2.7
10	19	20.9	1.2	46	2.9
11	23	22.0	1.4	45	4.3
12	20	22.9	1.3	45	4.3
13	8	23.4	1.5	46	4.0

TABLE 4.—*Percentage Relationship of Transverse Diameter of the Heart to Height*

Boys				Girls		
Number of Cases	± Standard Deviations	Percentage Relation of Heart to Height	Age	Percentage Relation of Heart to Height	± Standard Deviations	Number of Cases
5	0.2	8.3	2	8.3	0.4	4
5	0.6	8.1	3	8.4	0.5	9
20	0.6	8.2	4	8.4	0.5	21
31	0.6	8.1	5	8.0	0.5	31
30	0.4	7.9	6	7.8	0.4	25
27	0.5	7.7	7	7.5	0.5	31
29	0.6	7.5	8	7.3	0.5	28
33	0.5	7.3	9	7.2	0.5	23
17	0.5	7.2	10	7.1	0.5	18
20	0.6	7.1	11	6.9	0.7	23
16	0.6	7.2	12	7.0	0.6	21
7	0.4	7.0	13	6.8	0.7	7

SHAPE OF THE HEART

We have found that normal hearts in children fall naturally into four groups which correspond exactly to the four types of adult heart described by Hirsch and Shapiro.[6] These writers described a type of

6. Hirsch, I. S., and Shapiro, L. L.: Am. J. M. Sc. **162**:892 (Dec.) 1921.

heart which is characteristic of each one of the four main types of body build—the short, broad heart of the person with a hypersthenic habitus; the long, thin heart of the person with an asthenic habitus; the true drop heart of the person with a hyposthenic habitus, and the most common type of all, that belonging to the person with a sthenic habitus.

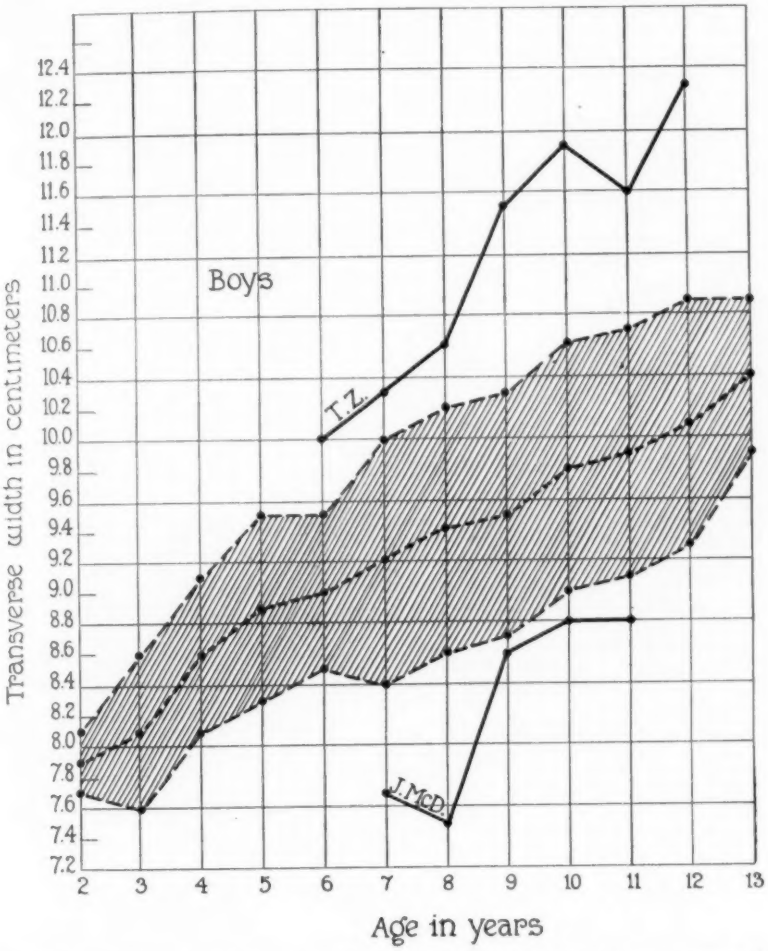

Fig. 1.—Normal variation of transverse width of heart in boys, compared with a case of large heart (T. Z.) and small heart (J. McD.). In this and in figure 2, the broken line shows the average transverse width; the diagonal lines, the average transverse width plus or minus standard deviations.

All our evidence points to the fact that while the types of heart in children are the same as in adults, they do not bear a constant relationship to the type of body build. The types of children's hearts are apparently determined early in growth, and they rarely change during the

age period which we have studied. It is possible to speculate endlessly on this subject. It may be that habitus is not constant until after adolescence or until full physical growth has been attained, whereas the types of heart remain constant in the great majority of cases. If this is so, it should be possible in a certain proportion of cases to be

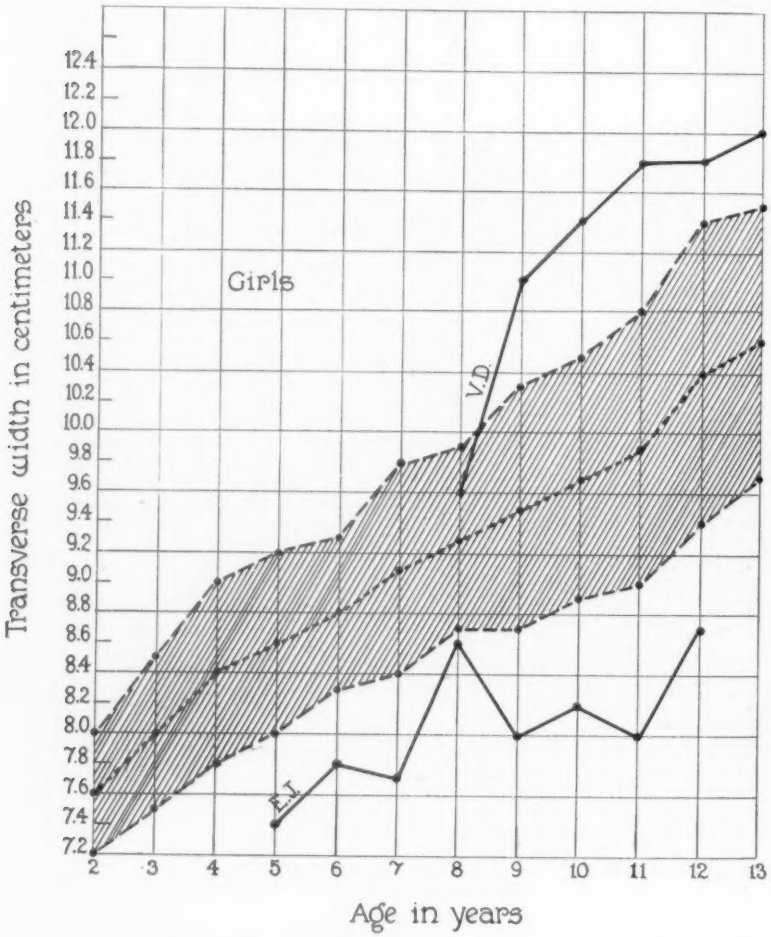

Fig. 2.—Normal variation of transverse width of heart in girls, compared with a case of large heart (V. D.) and small heart (E. J.).

able to predict the habitus of the adult from a roentgenogram of the heart in early childhood.

We studied the shape of the heart in a total of 788 roentgenograms of 246 children, fifty-six of whom had from four to seven roentgen-ray examinations in yearly succession.

The method of study was to designate each apparent new type of heart which was found by a letter of the alphabet. Thus the shape of heart on the first roentgenogram which was examined was called *A*. Heart shadows differing appreciably from this shape were designated *B*, *C*, and so on. These letters are not advocated as a nomenclature, but are simply symbols which we used for convenience in our own study. At first we thought we had twelve different shapes, but after long study of the roentgenograms rearranged in serial groups, we realized

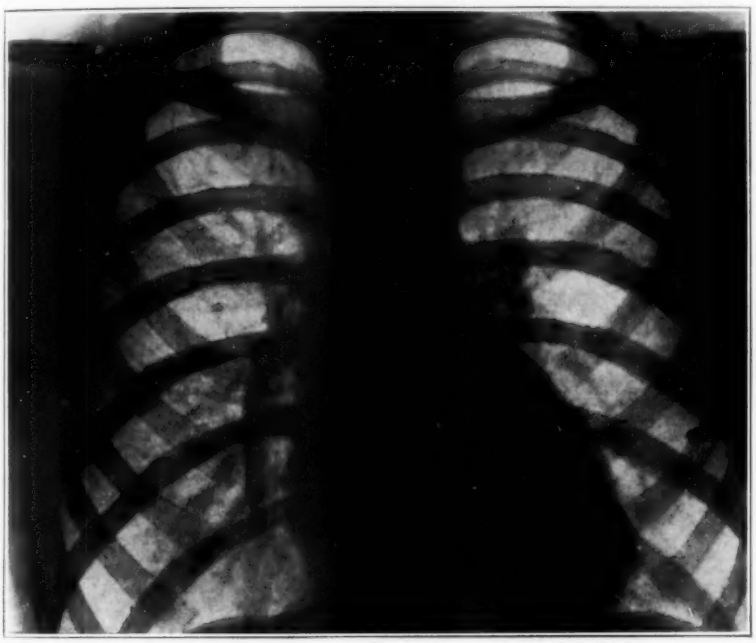

Fig. 3.—The *A* heart, corresponding to the sthenic heart of Hirsch and Shapiro.

that we were actually dealing with the four main types of Hirsch and Shapiro and with three common variations of the sthenic heart.

A, the most common type, occurring in 166 of our 246 cases, is the sthenic type of these writers. We described this type as having a moderately convex right side with approximately from one-fourth to one-third the diameter of the heart to the right of the midline. The left side is practically a straight line about 60 degrees to the horizontal. Seventy-five per cent of the cases showing *A* type hearts were in series and of these *A* was constant throughout in 57 per cent. The common variations of *A* we called *H*, *I* and *J*. *H* is by far the most usual variation, occurring in sixty of our cases. It differs from *A* in having

a more prominent right side (fig. 5). In series of roentgenograms of twenty-one children, *H* appears as the only type. Two children with orthostatic albuminuria, whose cases we followed through adolescence and the disappearance of symptoms, had constant *H* hearts. *I* and *J* are less common variations of *A*, occurring only eighteen and fourteen times. They were also constant in series in about one third of the cases. *I* differs from *H* in that the prominence of the right side is nearer the base of the heart, and in *J*, the right side falls in a straight line from the apex of the prominence to the diaphragm.

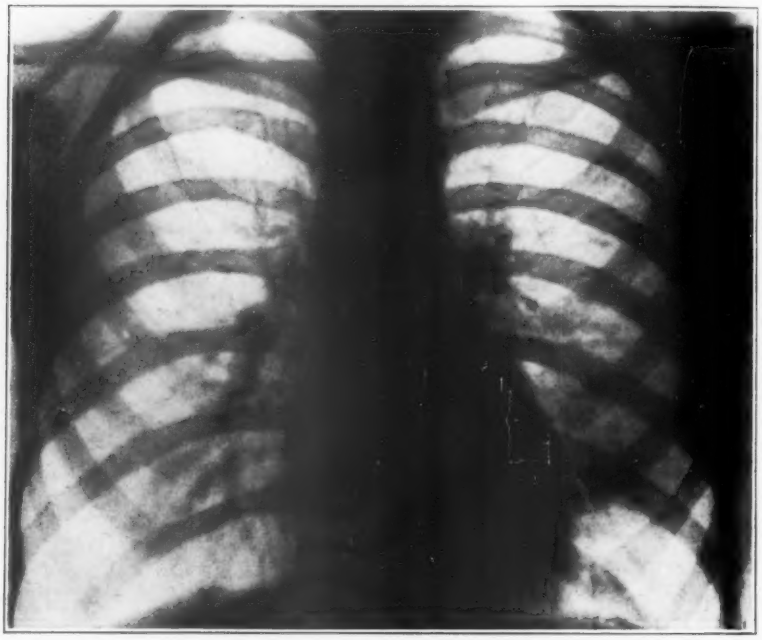

Fig. 4.—The *C* heart or hyposthenic type.

C, "like *A* but narrower," with the upper left border nearly vertical, is the asthenic heart of Hirsch and Shapiro's classification. The heart is on the diaphragm and not suspended. This is a relatively uncommon type, occurring in only eleven children. The belief seems prevalent that this type of heart is frequently associated with functional cardiac insufficiency. Of the eleven children, five boys and six girls, who showed this type of heart, only one had any symptoms referable to the circulatory system. None of them showed abnormal pulse rate or blood pressure at any examination. *C* is a type found more commonly in the older children of our series. The average age at which it was found was 10 years. It was found in two children of 5 years

and in two of 6 years, but the rest were 9 years or over. Seventy-seven per cent of the *C* type hearts found in series remained constant; the rest developed from *A* type hearts and then remained constant *C* hearts.

K, "like *C* but extremely narrow," and suspended over the diaphragm, is the hyposthenic heart, apparently rare before adolescence, as we saw it in only one child, a girl of 11.

"The broad, squat heart," which we classified as *D*, is apparently the hypersthenic heart of the adult. It occurred in twenty-one children in our group. This is distinctly a young type of heart; the average age

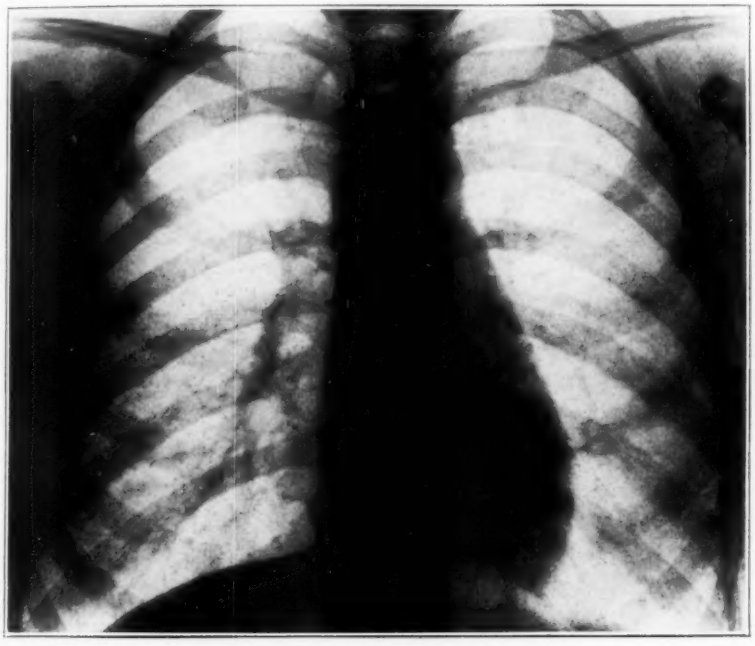

Fig. 5.—The *K* heart or asthenic type.

at which it occurred was only 5 and it was not seen in any child older than 9. Ten children having this type of heart eventually developed *A* type hearts.

Examples of these four main types of hearts and the three common variations of *A* are shown in figures 3, 4, 5, 6, 7, 8 and 9.

In serial examinations, it was common to find interchange from one of the variations of a type to another. In fact, it was not unusual in a series of from five to seven roentgenograms of the same child to find illustrations of all the variations of the common *A* type, but changes to the other main types were extremely uncommon. Of the 171 chil-

dren of whom at least two roentgenograms were made, only thirteen changed from one type to another. It was impossible to relate a change in the type of heart to a change in habitus. No change in habitus occurred in any of these thirteen children at the time of the radical changes in the shape of the heart. For example, in ten of the

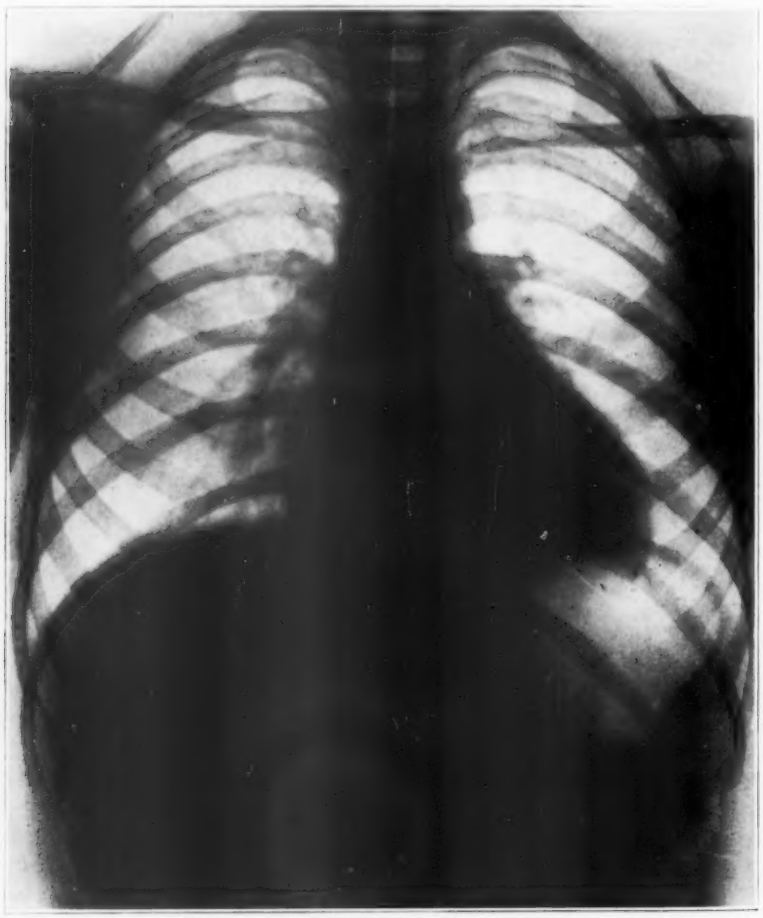

Fig. 6.—The *D* heart or hypersthenic type.

cases, the youthful type of broad heart, which we have called *D*, changed to the common *A* type at an average age of 6½ years, and further changes were not noted in the children. Every variety of physical type was represented in this group, both before and after the change in the shape of the heart. The other three cases in which a change in type occurred were in girls, the shape of whose hearts changed from the common type *A* to the long, thin heart (*C*) at an

average age of 10 years. Only one of these subjects approached the true asthenic type. Another girl was a true hypersthenic type, 20 per cent overweight, with a high chest-height ratio at the time of her change to a *C* type heart, whereas the third subject was a sthenic type of average height and weight and chest-height ratio. Equally negative results were obtained in all attempts to relate type of heart to habitus.

As noted before, the records of four children were omitted from all our statistics because they were known cases of mitral disease when

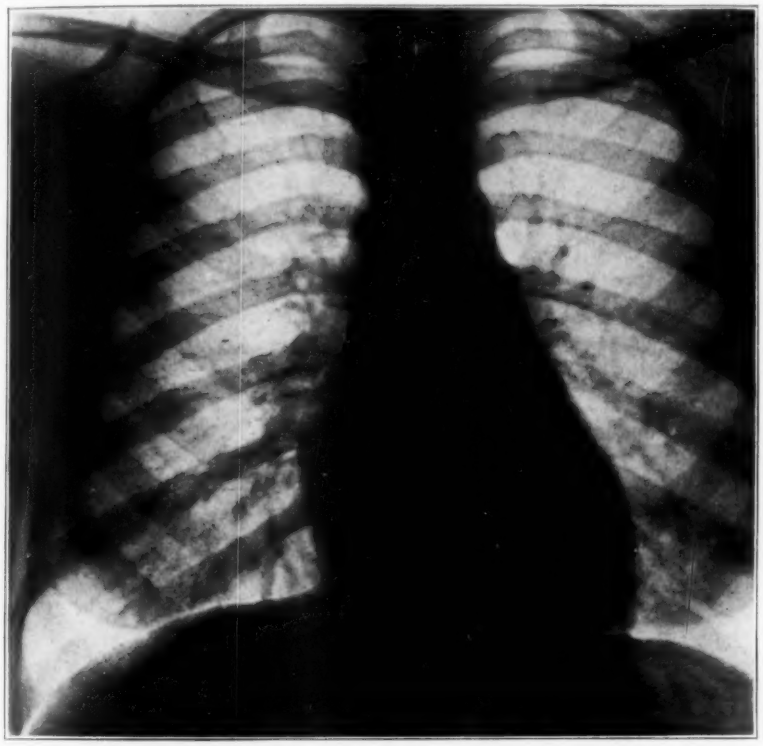

Fig. 7.—The *H* heart.

they entered the school. It is interesting to observe, however, that none of the children showed any abnormality in the shape of the heart (fig. 10). On the other hand, we had four normal children who showed marked accentuation of the pulmonary artery as well as the *H* variation illustrated in figure 7. This combination resulted in an outline which led at least two skilled roentgenologists to diagnose these four cases as typical mitral disease, although prolonged observation proved the hearts to be normal.

ACCENTUATION OF THE PULMONARY ARTERY

It is usual in reading roentgenograms to note the presence of an accentuated pulmonary artery, and a marked accentuation has been considered pathologic and suggestive of organic heart disease. In our series we found the pulmonary artery accentuated in 20 per cent of all the roentgenograms and markedly accentuated in 1.3 per cent. Some children never show a visible pulmonary artery,

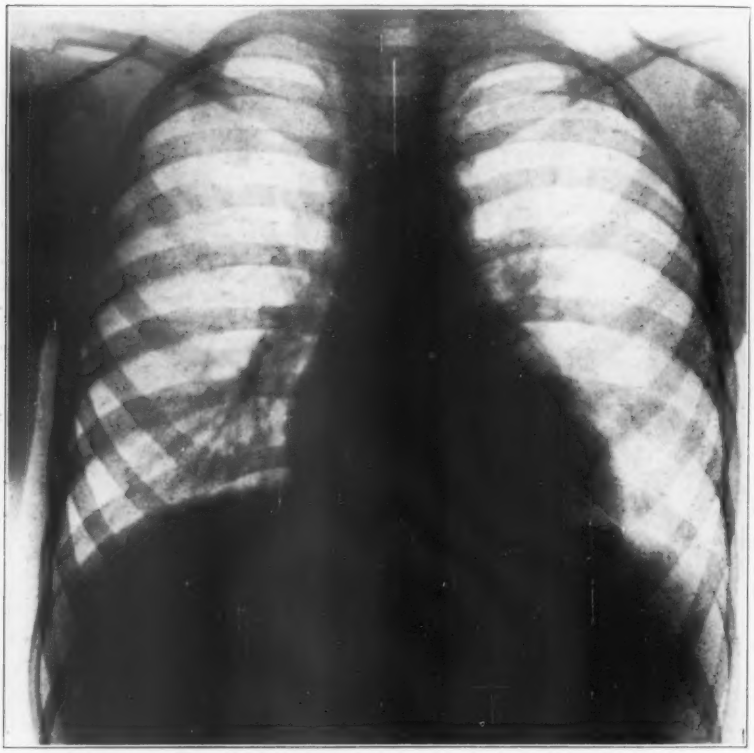

Fig. 8.—The *I* heart.

and in some, it remains marked throughout a series. This observation is apparently of no clinical significance, at least in our group of children, and we could not relate it to any symptoms or signs suggestive of cardiac disease. The most marked accentuation of a pulmonary artery which we found is shown in figure 11.

EFFECT OF RESPIRATION ON THE SHAPE OF THE HEART

As already noted, most of the roentgenograms we studied were made during moderately full inspiration. We therefore had little opportunity to study the effect of respiration on the shape of the heart. It is

of interest to note, however, that in one child the heart was found to be of uniform shape (*A*), with the exception of one observation which differed so markedly from the rest of the series that for a time the identity of the roentgenogram was in question. On reexamination we found that the shape of the heart could be changed at will from an *A* to a *D* type heart by having the boy inhale or exhale (figs. 12 and 13). We then reexamined a small group of other children and could not find any respiratory change, but none of the other children showed a wide excursion of the diaphragm. While our material on the subject

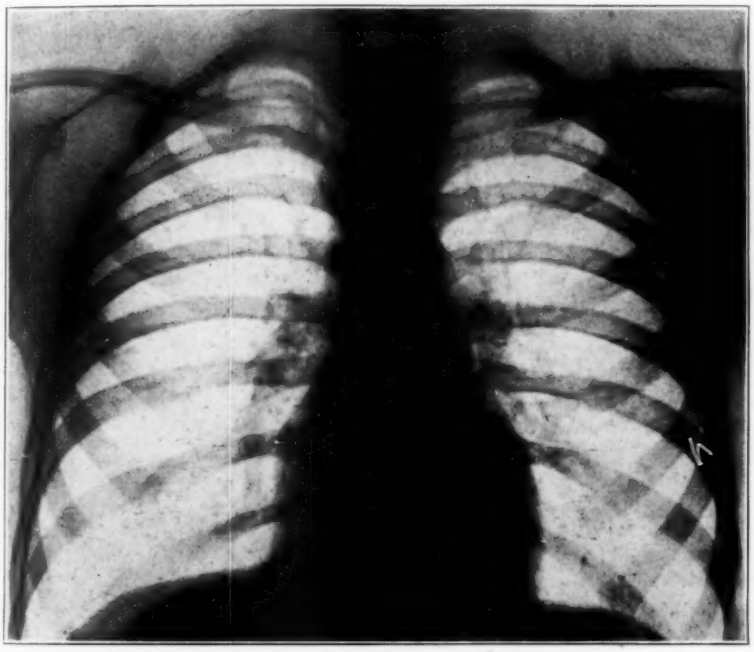

Fig. 9.—The *J* heart.

is limited, it seems likely that the discrepancy in the literature on the effect of respiration on the shape of the heart can be explained on the basis that a large rise of the diaphragm on expiration pushes the heart up into a transverse position, while this is not true of a slight excursion. An example of this is seen in figure 2 in the apparent increased diameter of E. J.'s heart at 8 years of age, which was due to a wide excursion of the diaphragm. Le Wald and Turrell [7] showed that in different phases of respiration the same heart at different times may vary as much as 3 cm. in transverse width, but that usually with

7. Le Wald, L. T., and Turrell, G. H.: The Aviator's Heart, Am. J. Roentgenol. **7**:67 (Feb.) 1920.

normal, quiet respiration, the changes in the transverse diameter are comparatively small, notwithstanding fairly large excursions of the diaphragm.

SERIAL RESEMBLANCES

The hearts of children frequently show so much individuality that the identity of the child can be established at once in succeeding roentgenograms. Occasionally, the serial pictures are so uniform in shape that they are practically identical. Examples of the few cases

Fig. 10.—This girl had a definite mitral regurgitation.

in which the contour of the heart varied markedly occur in the few children in whom a complete change of type took place, and in the occasional child who showed marked respiratory change in shape. De Buys and Samuel also noted many striking likenesses in successive roentgenograms of the same children.

FAMILY RESEMBLANCES

We found strong familial resemblances in roentgenograms in at least one half of our family groups. In fact, in a good many of the roentgenograms, the outlines of the heart looked more alike than the children did. This was found as commonly in siblings of different

sexes as in siblings of the same sex. There was a marked tendency for an accentuation of the pulmonary artery to occur in several members of the same family and again to be absent in all members of a family group.

SMALL HEARTS

Hearts with small transverse diameters were found in 3.6 per cent of our cases, and we were unable to relate these facts to any other physical condition, nor were we convinced that the small heart is a clinical entity as is the growth hypertrophy. In all but one of our

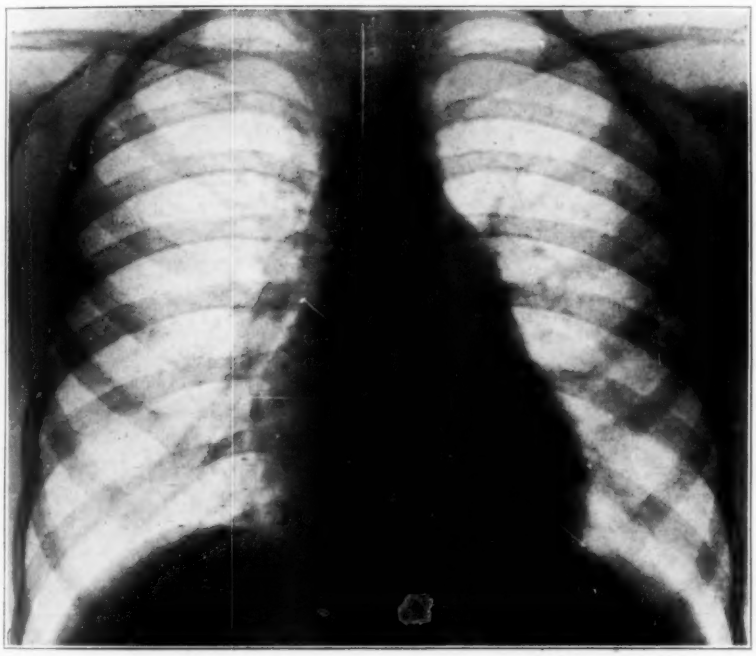

Fig. 11.—This girl showed the most prominent pulmonary artery shadow in our series.

cases, the condition was evident in the first roentgenogram, a point in favor of Adler and Krehbiel's [8] theory that microcardia is congenital. Although others have emphasized the fact that small hearts occur less commonly in boys, in our series there were five boys and four girls. Adler and Krehbiel noted that there were rarely symptoms relating to the circulatory system, but that gastric and nervous symptoms were common. One boy in our series had dyspnea on moderate exercise over

8. Adler, I., and Krehbiel, O. F.: Orthodiascopic Observations Concerning a Certain Type of Small Heart and Its Relation to Some General Systemic Affections, Arch. Int. Med. **9**:346 (March) 1912.

a period of two years, but nervous or gastro-intestinal symptoms were not found in any subject. Correlation could not be made between the small heart and physical observations. In most cases, the blood pressure and pulse rates were near the average. Occasionally, a high or low blood pressure and a slow or rapid pulse appeared transiently. One boy showed a slow pulse rate on all examinations.

In eight of the nine children, the small heart was not of the asthenic type, but was really a sthenic heart in miniature.

The children were all overheight with three exceptions, two of whom were of normal height and one of whom was decidedly short. The ratio

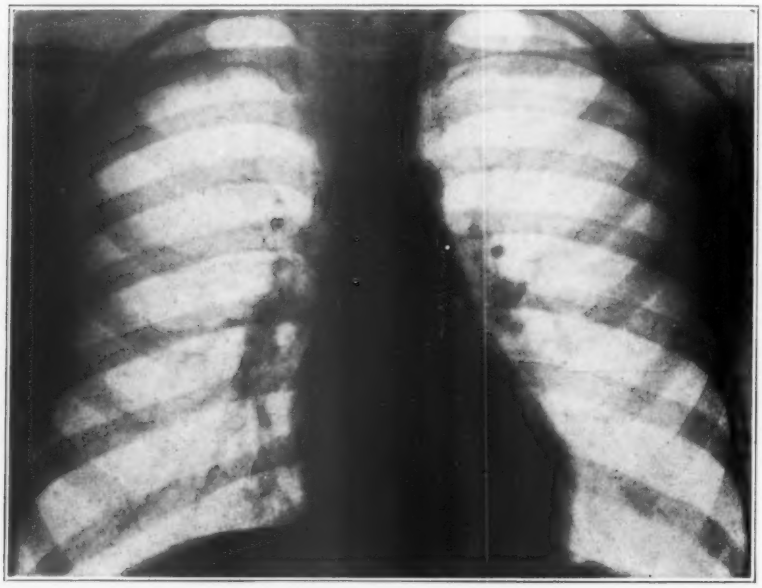

Fig. 12.—Illustrating a case of extreme effect of respiration on the shape of the heart shadow (See fig. 13).

between height and the width of heart was nearly normal in the last case, but was low in all the children who were overheight. The ratio between the width of the heart and internal diameter of the chest remained normal in all of the cases except in the two girls who ultimately developed hearts of the *C*, or the asthenic, type. In both of these cases the chest-heart ratio remained low, so that these were really small hearts in chests of average size, whereas the others were small hearts in small chests. With the exception of these cases, the width of the heart tends to approach the normal with increase in age, although the measurements still remain below the average figures. There were no constant changes in the electrocardiograms of the children with small hearts.

LARGE HEARTS

When the clinician finds a case of cardiac hypertrophy, he is most anxious to be able to determine whether or not the size of the heart is of pathologic significance in the particular case he is studying. Large hearts, if associated with other symptoms and signs of heart disease, usually mean an organic cardiac lesion. But Krehl [9] has described a certain type of cardiac hypertrophy occurring without known cause in young persons. He designated this condition as "growth hypertrophy," and believed that the enlargement of the heart was due to the rapid growth of the body. In 1913, Bass and Wessler [10] described similar

Fig. 13.—Same boy as in figure 12; deep expiration.

cases in children above the age of 9 and used the term "juvenile heart." Of the 246 children we have studied, there were twenty-one girls and twenty-one boys whose transverse cardiac diameters at any time exceeded the normal limits as determined by the standard deviations. Many of these were children whose measurements on successive examinations were near the high level of normal and who exceeded the limit on only a single roentgenogram. Only eleven of the forty-two children showed hearts which were larger than normal on two or more

9. Krehl, L.: Die Erkrankungen des Herzmuskels und die nervösen Herzkranheiten, Spec. Path. u. Therap. Nothagel, Wien. **15**:391, 1901.

10. Bass, M., and Wessler, H.: Heart Size and Heart Function in Children showing Orthostatic Albuminuria and Orthodiagraphic Study, Arch. Int. Med. **11**:403 (April) 1913.

examinations. Every one of these showed exactly the established characteristics of the "juvenile heart." An example of this type of heart is illustrated in figure 14, which shows the transverse position and rounded apex which, as well as the increased transverse diameter, are characteristic of left ventricular hypertrophy. It is possible that heredity plays some part in the determination of this phenomenon. At least in our small group there are two brothers and two sisters who showed the same characteristics. In addition, a younger brother of a boy in this group had a heart of normal size until the last year of our study, when at 6 years his heart increased 1.4 cm. in transverse width.

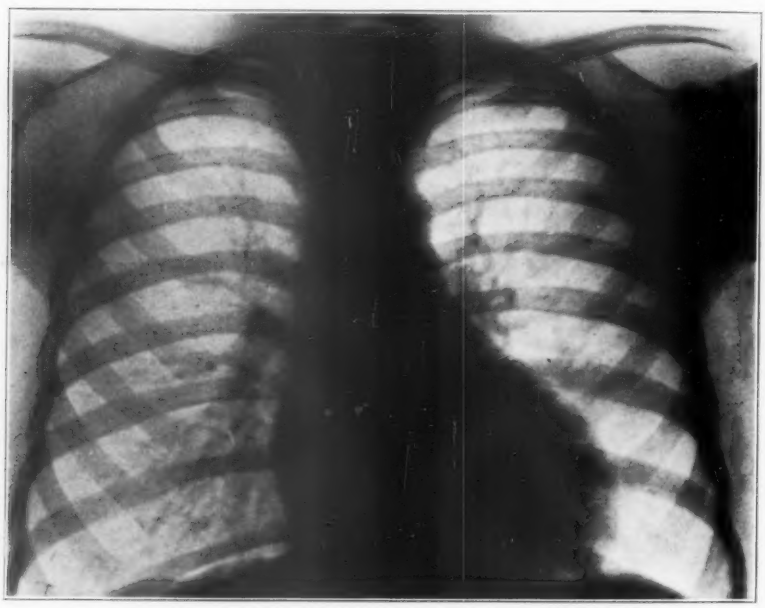

Fig. 14.—The "growth hypertrophy" or "juvenile heart."

Because of the characteristic shape of his heart on this last examination, it is likely that he will have a juvenile heart.

Simple hypertrophy of the heart was disclosed in our series of roentgenograms in children as young as 5 years of age, but the clinical picture of increased percussion to the left, displacement of the point of maximum impulse outside the mammillary line and heaving apical impulse was not apparent in any child before 9 years of age. The probable reason why Bass and Wessler and others have not reported cases in children under 9 years old is that there is rarely anything in the physical examination of the heart which would call for a roentgenogram, and so these cases go unnoticed unless, as in our series, routine yearly roentgenograms are being made. The clinician must bear in

mind, however, that growth hypertrophy may occur even in young children, and that a large heart in a young child does not necessarily mean a pathologic condition, especially if there are no symptoms nor other signs of cardiac hypertrophy.

In our series of six girls and five boys, the condition was discovered by teleoroentgenograms, in two children at 5 years, in three, at 6 years, and in three more, at 7 years of age. The youngest child who showed physical signs of left ventricular hypertrophy was 9 years old, and all examinations of children older than this showed the typical clinical picture. None of the boys had symptoms such as dyspnea, pallor, cyanosis or undue fatigue on exertion. Two of the girls also did not show symptoms, notably the girl with the largest heart. Two other girls showed marked vasomotor instability with attacks of fainting only as they approached adolescence. The remaining two girls had slight cyanosis and marked fatigue on moderate exertion during the first two years in which the growth hypertrophy was evidenced by their roentgenograms. During this time, their hearts were not only large, but disproportionately large for the chest and height, and when these ratios again became normal, all symptoms disappeared.

An intensive study of the clinical conditions in these children showed that only two of the girls had transient murmurs, and in all cases, the blood pressures, pulse pressures and pulse rates did not reveal constant factors; apparently the physical examination in early life is of no help in determining whether a child is suffering from a growth hypertrophy or from a true valvular lesion.

After finding that the correlation of the width of the heart with height was greater than with age, we naturally questioned whether we were not simply dealing with tall children who had hearts large for their ages but not for their heights. But the transverse diameters of the juvenile hearts exceeded the normal ratios to height as well as the average heart width for age. The growth hypertrophy at first showed large hearts in proportion to their chest-width; as the condition became established, however, the chest-heart ratio once more became normal—a large heart in a large chest.

The electrocardiogram did not help us in the diagnosis of growth hypertrophy in children. None of our children showed a ventricular preponderance of the left side, and there were no other definite diagnostic features, save possibly the fact that the R wave was notched or split a little more frequently in these children than in the rest of our group.

CONCLUSIONS

1. The average median diameter of the right side of the heart increases steadily with age in children from 2 through 13 years of age, being greater in girls than in boys at the extremes of the age groups.

2. The average median diameter of the left side of the heart increases steadily with age in children of from 2 through 13 years, with no sex differentiation.

3. Until the age of 7, the girls' hearts are smaller than the boys, but after 11, this condition is reversed.

4. The longitudinal diameter of the heart was not found of value in estimating the size of the heart.

5. The transverse width of the heart varies from 7 to 8.2 per cent of the height in boys of from 2 through 13 years, and from 6.9 to 8.4 per cent of the height in girls of the same ages.

6. There is a closer correlation between height and the size of the heart than between age and the size of the heart.

7. Approximately one third of the heart lies to the right of the midline in children from 4 through 13 years of age.

8. The transverse diameter of the heart is approximately one half of the width of the chest in children from 2 through 13 years of age, and there is no change in this relation with increasing age or height.

9. There are four main types of the shape of the heart in children as in adults, but the shape of the heart in children does not bear a constant relationship to the type of body build.

10. Changes from one type of heart to another are uncommon, occurring in only 0.6 per cent of our cases.

11. The drop heart is extremely rare in children from 2 through 13 years of age, occurring in only one of our cases.

12. Accentuation of the pulmonary artery, even when marked, has not had any pathologic significance in the cases studied.

13. The effect of respiration on the shape of the child's heart appears to depend on the extent of the diaphragmatic excursion.

14. Serial roentgenograms of the same child usually show great uniformity in contour of the shadow of the heart.

15. There is a strong, familial resemblance in the shadow of the heart in one half of our family groups.

16. Microcardia occurred in 3.6 per cent of our cases and was of little or no clinical significance. There was a tendency for the heart to become of normal size at the approach of adolescence.

17. Roentgenograms disclosed growth hypertrophy in children as young as 5 years who did not show any clinical evidence of this condition until they reached the age of 9.

VITAMIN REQUIREMENTS OF NURSING YOUNG

II. THE PRODUCTION OF BERIBERI IN THE NURSING YOUNG (MUS NORVEGICUS ALBINUS) ASSOCIATED WITH HEMORRHAGES *

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In previous publications, one of us (B. S.)[1] presented extensive evidence that the vitamin B requirements for normal lactation are at least three times as great as that for optimum growth. Recently he demonstrated that the large requirements of vitamin B for lactation are due to the inability of the nursing mother to secrete vitamin B quantitatively in the milk, since only a fraction of the vitamin B intake of the lactating mother is transferred by the mammary gland to the milk.[2] In this communication, we report further work which corroborates the former observations and we also report observations made on certain pathologic lesions encountered in the polyneuritic state of the nursing young of the albino rat which have received inadequate amounts of vitamin B, namely, hemorrhages in the osteogenetic tissues and in certain of the viscera.

A preliminary report of this work was presented before the American Society of Biological Chemists in April, 1927.[3] In the meantime the work of Moore, Brodie and Hope [4] appeared, showing subcutaneous, visceral and intracranial hemorrhages in polyneuritic nursing young.

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* From the Departments of Agricultural Chemistry and Veterinary Science, University of Arkansas.

* Research Paper No. 60, Journal Series, University of Arkansas.

1. Sure, Barnett: Vitamin B Requirements for Normal Lactation, J. Biol. Chem. **74**:55 (July) 1927; A Quantitative Method for the Study of Vitamin B Requirements for Lactation, ibid. **76**:673 (March) 1928.

2. Sure, Barnett: Vitamin Requirements of Nursing Young: 1. The Unusual Response of Nursing Young (Mus Norvegicus Albinus) to Vitamin B Administrations, J. A. M. A. **89**:675 (Aug. 27) 1927.

3. Sure, Barnett; and Schilling, S. J.: The Production of Beri-Beri in the Nursing Young on Diets Entirely Adequate for Growth, Proc. Am. Soc. Biol. Chem. **74**:74 (July) 1927.

4. Moore, U. C.; Brodie, J. L., and Hope, R. B.: Some Effects upon the Young of Inadequate Maternal Diets: 1. Polyneuritis and Hemorrhages, Am. J. Physiol. **82**:350 (Oct.) 1927.

Moore and Brodie [5] have also since reported a case in an infant who died of beriberi with accompanying hematuria, the mother's prenatal diet having been markedly deficient in vitamin B.

Since the completion of this work our attention has also been called to a paper by Shipley, McCollum and Simmonds [6] entitled "Lesions in the Bones of Rats Suffering from Uncomplicated Beriberi," which was published as one of a series of articles on studies of rickets. In this paper, microscopic evidence is presented showing that rats (after weaning) fed on a diet which is complete except for the absence of the antiberiberi factor develop lesions in the bones which are essentially identical with those seen in guinea-pigs suffering from acute and uncomplicated scurvy.

In this work six comparable rations, the composition of which is indicated in table 1, and the footnote of table 6, rations which were

TABLE 1.—*Composition of Rations Containing Varying Proportions of Defatted Wheat Embryo as the only Source of Vitamin B* *

Ration Number	Commercial Casein	Agar-Agar	Salts No. 32	Ferric Citrate	Defatted Wheat Embryo	Wheat Oil	Dextrin
891	20.0	2.0	4.0	0.25	10.0	3.0	60.75
892	20.0	2.0	4.0	0.25	15.0	3.0	55.75
898	20.0†	0.0	4.0	0.0	20.0‡	3.0	53.0
899	20.0†	0.0	4.0	0.0	10.0‡	3.0	63.0
863	20.0	0.0	4.0	0.25	20.0	3.0	52.75
868	20.0	0.0	4.0	0.25	30.0	3.0	42.75

* 0.3 cc. of cod liver oil was administered daily to each animal separately from the ration.
† Washed for a week with dilute acetic acid.
‡ Ether-extracted wheat embryo secured from Washburn-Crosby Milling Co., Minneapolis. All the rest of the wheat embryo used in this investigation was secured from near Indianapolis, and was supplied by the research laboratories of Eli Lilly and Co.

similar except with regard to their content of a source of vitamin B, were fed to eighteen females. The work extended over 244 days, during which time thirty litters consisting of 258 young became available for observation. Since experiments on rations 891, 892, 898 and 899 were carried on for relatively short reproduction periods, the results of such diets on fertility are not as extended. Table 2 gives a summarized account of the success encountered in the rearing of young on the various rations and shows that satisfactory results in lactation were obtained only on rations containing 30 per cent of defatted wheat embryo as a source of vitamin B. In the interpretation of these results,

5. Moore, U. C., and Brodie, J. L.: The Relation of the Maternal Diet to Hemorrhage in the New-Born, Am. J. Dis. Child. **34**:53 (July) 1927.

6. Shipley, P. G.; McCollum, E. V., and Simmonds, N.: Studies on Experimental Rickets: IX. Lesions in the Bones of Rats Suffering from Uncomplicated Beri-Beri, J. Biol. Chem. **49**:399 (Dec.) 1921.

it should be noted that we found that a diet furnishing 10 per cent of the total ration in the form of wheat embryo defatted with acetone, as a source of vitamin B, permits good growth. Increasing the proportion of defatted wheat germ to 20 per cent produces excellent growth far superior to the Donaldson standard, but is inadequate for lactation. Further increase of the concentration of wheat germ to 30 per cent in the ration results in normal lactation, as shown in table 2.

TABLE 2.—*Record of Fertility and Lactation of Females on Rations, the Composition of Which is Given in Table 1*

No. of Ration	Defatted Wheat Embryo (Per Cent)	Duration of Experiment (Days)	No. of Females	No. of Litters	No. of Young Born	No. of Young Born Alive	Young Allowed To Be Reared	Young Weaned	Percentage of Young Weaned	Comment
891	10.0	135	3	1	5	5	5	0	0	Litter disposed of by mother in a few days
892	15.0	115	2	2	20	20	12	0	0	Young died of beriberi on thirteenth to twentieth day of lactation with milk in their stomachs
898	20.0	127	3	3	27	27	18	0	0	Necropsies performed on a majority of the dying and dead young and invariably milk was found in their stomachs. The young died of beriberi
899	10.0	129	3	3	28	28	18	0	0	Two litters disappeared early during lactation; the third litter removed from the mother for observation when it was in a dying condition on the eighteenth day of lactation
896	20.0	244	3	10	90	89	59	11	18	Postmortem examinations made of all the young that died of beriberi; all the young found with milk in their stomachs
868	30.0	244	3	10	83	83	52	50	96	Note the remarkable success in lactation due to the larger proportion of defatted wheat embryo in raton

Another angle of approach to the question of the quantity of vitamin B which must be fed to the lactating female in order to satisfy the requirements for successful lactation is the feeding of controlled quantities of potent sources of this vitamin to the previously depleted lactating female and noting the results. This was done and is reported in table 6, from which may be noted that 750 mg. of Harris yeast administered daily to the lactating mother, after she has depleted her vitamin reserves, is inadequate for rearing of the young. We have

since found that a daily allowance of 1,500 mg. of this yeast to the mother permits normal lactation, although excellent growth in the adult is secured with a daily dosage of only 500 mg.

Certain clinical observations were made on numbers of failing young. Some of these are given in tables 3 to 6, inclusive. Necropsies also were performed as far as possible, and in them the scope of the observations were extended as the work progressed. Since the

TABLE 3.—*Data of Female 3,853 on Ration 866 of the Second Litter in Which Seven Young Were Born, Six of Which Were Allowed to Be Reared (Disposed of First Litter on Second Day of Lactation)*

Date	Weight of Female (Gm.)	Weight of Litter (Gm.)	Comment
1926			
12/26	241	...	
12/28	202	32	One young was dragging its hind legs at 10 a. m. on Jan. 18, 1927, and died between 1:00 and 1:30 p. m. on the same day; weight, 17 Gm.
12/30	...	35	
1927			
1 / 1	...	47	
1 / 3	...	62	Necropsy:
1 / 5	...	76	Hemorrhagic appearances in junctures of cranial and facial bones, sternum, ribs, vertebrae, femur, tibia and digital bones; kidney appeared congested; stomach full of milk
1 / 7	...	88	
1 / 9	...	108	
1 /11	...	116	
1 /12	...	119	Rest of young all nursing at 3:00 p. m., and mother showed maternal instinct
1 /13	...	125	
1 /15	...	132	
1 /16	182	134	Another young died at 8:50 a. m. on the 19th.; still able to walk around but dragging its hind legs at 8 a. m.; completely paralyzed five minutes before death
1 /17	...	132	
1 /18—10:00 a. m.	...	132	
1 /18— 2:30 p. m.	...	112(5)*	
1 /18— 4:30 p. m.	...	111(5)*	Necropsy:
1 /19— 8:00 a. m.	...	103(5)*	Stomach full of milk; hemorrhagic appearance along junctures of cranial and facial bones, sternum, femur, tibia, digital bones and vertebrae
1 /19— 8:50 a. m.	...	87(4)*	
1 /20	...	57(3)*	
1 /21	...	35(2)*	Another young found dead on the morning of the 20th; partly consumed; one young died on the 20th; at 5:00 p. m. of the 21st the two remaining young of this litter still alive and had muscular control of their hind legs; one died during the night and the other had muscle chills and was paralyzed at 10 a. m. on Jan. 22; postmortem examination showed milk in the stomach.

* Number of young alive on date indicated.

primary object of this study related to vitamin B requirement during lactation, it was not attempted to obtain necropsies on those young which died in the first few days after birth. Such young probably may be considered as laboring under some handicap largely referable to disturbances during the period of gestation. Moreover, the animals which died early were frequently consumed by the mother and thus did not become available for further study. Also, deaths often occurred when it was not possible to obtain the postmortem data; again, some of the animals died during the night and thus the observation on paralysis or muscular tremors (chills) were not secured.

PARALYSIS, CHILLS AND CYANOSIS

Paralyses, muscular tremors and cyanotic conditions have for a long time been recognized as part of the symptom complex accompanying beriberi. Partial to complete loss of control of the rear limbs was observed with great regularity among the failing young. The latter condition commonly developed only a few hours prior to death. The muscular tremors regularly developed later than the paralysis of the rear limbs, while cyanosis appeared last, was absent in animals

TABLE 4.—*Data of Female 3,980 on Ration No. 898 of the First Litter, in Which Six Young Were Born, All of Which Were Allowed to Be Reared*

Date	Weight of Female (Gm.)	Weight of Litter (Gm.)	Comment
1926			
11/20	214	...	
11/21	170	28	Necropsy:
11/22	...	28	First young that died during night of December 8;
11/23	...	30	stomach full of milk; hemorrhagic condition of
11/24	...	33	junctures of cranial bones and of vertebrae, tibia
11/25	...	37	and femur
11/27	...	47	Second young died during day of December 10;
11/29	...	61	stomach full of milk; hemorrhagic condition of
12/ 1	...	75	junctures of cranial bones and vertebrae, tibia
12/ 2	...	85	and femur; petechiae in thymus
12/ 3	...	93	
12/ 4	...	103	Third young in dying condition during day of
12/ 5	...	112	December 10; posterior paralysis advanced; chloro-
12/ 6	...	122	formed
12/ 7	...	132	Necropsy:
12/ 8	...	137	Stomach full of milk; kidney congested; vertebrae
12/ 9	...	124(5)*	hemorrhagic; congested condition in junctures of
12/10	...	80(3)*	cranial bones
12/11	...	25(1)*	
			On December 11, the only remaining young of the litter in a dying condition; weighted 23 Gm. in early morning; lost 2 Gm. in succeeding five hours, when it died; prompt necropsy
			Necropsy:
			Stomach full of milk; areas of congestion in liver; hemorrhagic conditon of junctures of cranial bones, digital bones, tibia and caudal vertebrae; no visible signs of hemorrhagic condition in sternum, ribs, or thoracic vertebrae

* Number of young alive on date indicated.

killed at the onset of the paralytic condition and was constant in those permitted to die or found dead. This fact, together with the observation that respiratory movements were intermittent and shallow in the last stages, suggests that death occurred from respiratory failure.

QUANTITY OF MILK IN STOMACHS

In thirty-two out of a total of thirty-five or in 91 per cent of the animals examined, all of which were nursing young, the stomach was found to be well distended with curd. We consider this to be concrete evidence that the reason for the failure during lactation of this group was due to a deficiency in the quality of the milk yielded

by the lactating mothers, rather than to an elaboration of insufficient quantity. These symptoms corroborate the clinical observations so frequently observed in our work that the mothers showed maternal instinct and that the young nursed until shortly before death, some nursing even when paralysis of the rear limbs had become pronounced (table 5).

HEMORRHAGES IN OSTEOGENETIC TISSUE

It was observed at an early period in this study that the failing young showed a uniform disturbance in certain tissues of the body. The abnormality noted was a hemorrhagic appearance occurring in the osteogenetic tissues along the junctures of the cranial and facial

TABLE 5.—*Female 3,950 on Ration 892 of the First Litter, in Which Ten Young Were Born, Six of Which Were Allowed to Be Reared*

Date	Weight of Female (Gm.)	Weight of Litter (Gm.)	Comment
1926			
11/ 7	214	...	
11/ 8	156	28	On morning of November 22, two young found dead and one practically devoured; one of the two young available for necropsy had milk in its stomach; remaining three showed disinclination to move about at 11 a. m., which condition was greatly intensified by 3 p. m.; observed nursing at 4 p. m., and at 4:30 p. m. developed posterior paralysis and muscle chills; they were observed in the laboratory until 9 p. m., when they were in dying condition; at this time the young chloroformed; all found to have milk in their stomachs; mother showed active secretion on following morning; small drops of milk could be squeezed out of the mammary glands
11/ 9	...	30	
11/11	...	42	
11/13	...	55	
11/15	...	69	
11/17	...	87	
11/18	...	98	
11/19	...	107	
11/20	...	117	
11/21	...	122	
11/22	183	68(3)*	

* Number of young alive on date indicated.

bones and in the interior structures of the tibia, femur, vertebrae, sternum, digital bones and ribs, in the last named, particularly, at the costochondral junctures. Observations on this point were made on thirty-one animals. Twenty-three of this group were nursing, their ages ranging from 15 to 26 days; six had been weaned, were 27 days old and were making moderate gains in growth; two others were stock rats, from 60 to 64 days old, which since weaning had been kept on a diet deficient in vitamin B and are here included for the sake of comparison.

The most common seat of this hemorrhagic disturbance appeared to be in the osteogenetic tissues along the junctures of the cranial and facial bones and in the tibias and femurs. In 97 per cent of the animals examined, distinct disturbance could be noted in these locations. If the two animals, from 60 to 64 days old, which had been weaned,

thus presenting a postlactation phenomenon, and which were in moderately good condition when chloroformed for necropsy, are excluded, the percentage of positive symptoms is 100. The percentage of other positive observations on hemorrhagic conditions in bones ranges from 84 per cent for the sternum, 77 per cent for the digital bones and thoracic vertebrae, 74 per cent for the caudal vertebrae to 54 per cent for the ribs. Other bones were not examined, except in one animal in which the mandible was dissected out and found to appear hemorrhagic.

The hemorrhagic condition of the cranial and facial bones was most commonly encountered and was most prominent at the juncture of the occipital with the parietal bones. The area was broadest at the median line of the skull and tapered off toward either side. The central parts of the parietal and occipital bones never were found to appear abnormal, and the line of demarcation between normal and hemorrhagic areas was sharp. The discoloration of the affected areas varied in breadth and in intensity, but was in all cases so distinct that difficulty was not experienced in distinguishing between conditions noted in the animals under discussion here and in normal rats of the same ages on which necropsies were performed also.

Hemorrhagic conditions along the junctures of the frontal and nasal bones occurred in a number of cases, at times being more prominent than, and at times occurring in the absence of, manifestations of disturbance in the cranial region. The condition of the cranial region, however, was found to be abnormal more frequently and the hemorrhagic area more extensive than in the facial region. Distortion of the cranial or facial bones was not observed.

While the incidence of hemorrhagic lesions was almost as great in the femur and tibia as in the bones of the skull, closer scrutiny was necessary in order to note the variation from the normal. These bones in animals of the age studied are translucent and normally are a pinkish gray when viewed by reflected light, and have a deeper pink cast when viewed by transmitted light. In the abnormal animals the bones appeared dark red or had a bluish or purplish cast by reflected light, and when they were viewed by transmitted light, the cancellated bone and marrow showed a distinctly red to purple color.

The incidence of hemorrhagic conditions in the sternum, thoracic vertebrae and especially in the ribs was somewhat more variable. In all animals, the sternum and ribs were examined by isolating a section of the wall of the chest and freeing it from the skin and superficial muscles, the bones then being held together by intercostal muscles; the preparation was washed and then viewed by transmitted light. The thoracic vertebrae were examined by laying aside the skin and

as much of the musculature as was required and viewing them by reflected light. Reddening of the central tissues of the ribs and sternum and of the bodies of the thoracic vertebrae as compared with normal rats of the same age was the criterion employed in determining the presence of lesions in these bones. In the ribs the lesions usually were most pronounced near their juncture with the costal cartilages. Rosary formation or abnormal curvature of the ribs was not observed.

Examination of the digital bones and of the caudal vertebrae was made with appropriate checks by transmitted light. In the case of the former, clear-cut distinctions between normal observations and those which we here describe as hemorrhagic were easily made in all animals except two. The latter animals were 60 and 64 days old, respectively, and the tissues of the foot were too dense to permit making proper observations. In the foot it was found that the phalanges gave the most easily observed index to hemorrhagic disturbance, while the metatarsi and metacarpi also yielded a considerable number of positive observations. Not all the phalanges, metatarsi or metacarpi of the same animal were equally affected; in most cases some individual bones would show prominent reddening, while others appeared normal. The examination of the caudal vertebrae in the older rats with thickened tissues of the tail was not found to be feasible, and in the younger animals direct comparison with normal rats was in some cases found necessary. In normal rats from 12 to 15 days old, tails viewed by transmitted light show a series of delicate pinkish zones, each representing a vertebra and separated from each other by more translucent and less colored portions which represent the intervertebral cartilages. Hemorrhagic conditions were observed as a deeper red and purple appearance of the individual vertebrae. It should be noted that if nursing animals only were included, the incidence of lesions in the caudal vertebrae would be 100 per cent.

To determine whether the hemorrhagic appearance in the bones described was due to actual hemorrhage or to congestion, sections were made from the tails of selected animals. These were stained with Delafield's hematoxylin and eosin and showed red corpuscles in large numbers outside of the vessel walls, i. e., true hemorrhages. The osteoid and osteogenetic tissues of the ends and of the lateral margins of the caudal vertebrae were not observed to differ from the normal, while the more pulpy osteogenetic tissue of the interior was the seat of the disturbance.

Since the question arose in our minds whether it was possible that the manner in which we disposed of the animals we killed or the opportunity for postmortem change in animals which died during the night could have had any influence in causing the appearances of

congestion in bony tissues, we killed eighteen normal young as controls to satisfy ourselves on the point in question. Some of these were suffocated, some chloroformed, and others were killed by means of strychnine. In some, necropsy was performed immediately; in others, it was performed after they were placed on ice, at room temperature, and at 37 C. in an incubator overnight. However, we did not observe in any case the development of changes which simulated the conditions found in the bones of the failing animals on the rations under investigation.

TABLE 6.—*Lactation Record of Female 4416, Transferred on Date of Birth of Litter from Stock Diet No. 1* to Ration 988† of the First Litter, in Which Eleven Young Were Born, Six of Which Were Allowed to Be Reared*

Date	Weight of Female (Gm.)	Weight of Litter (Gm.)	Comment
11/21	227	32	§ Number of young left on date indicated; a few days after birth, one runt developed; on November 29, weighed only 5 Gm.; on the following morning, found dead, leaving five in the litter; on the night of December 9, two more young died; on postmortem examination, both showed marked hemorrhagic condition at the juncture of occipital and parietal bones; a fourth young died on the night of December 10; one of the remaining two young had paralysis and chills on December 11; the animal was chloroformed and the hemorrhagic condition of the osteogenetic tissues forming the juncture of the occipital and parietal bones was photographed (animal 1, in illustration)
11/22	210	35	
11/23	212	38	
11/24	209	44	
11/25	207	49	
11/26	205	58	
11/27	192	63	
11/28	192	67	
11/29	187	77	
11/30	177	75(5)§	
12/ 1	173	79	
12/ 2	171	82 ¶	
12/ 3	179	86	
12/ 4	183	85	
12/ 5	183	87 ‡	¶ Began to administer daily 500 mg. of Harris yeast to mother (the yeast was triturated with 5 drops of cod liver oil to insure sufficiency of vitamin D)
12/ 6	187	92	
12/ 7	192	93	
12/ 8	198	87	
12/ 9	198	82	‡ Increased dosage of yeast to 750 mg. daily to mother.
12/10	207	47(3)§	
12/11	202	33(2)§	

* Composition of Stock Ration No. 1: Whole wheat, 27; rolled oats, 26; yellow corn, 25; oil meal, 15; commercial casein, 5; cod liver oil, 1; sodium chloride, 0.5; calcium carbonate, 0.5; and a liberal supply of fresh whole milk daily.

† Composition of Experimental Ration 988: Casein (purified), 20.0; agar-agar, 2; McCollum's salt mixture no. 185, 4; butter fat, 10; dextrin, 64.

‡ Note that after the administration of the yeast the mother is recovering her lost body weight, and is in excellent condition while the young are failing and later dying.

HEMORRHAGES IN INTERNAL ORGANS

Petechial hemorrhages in the internal organs and in the subcutis were encountered in the failing and dying young but with far less regularity than lesions in the bone. Thus, in the necropsies of thirty-one animals, hemorrhages in the spleen were recorded only twice; in the liver, nine times; in the thymus, once; in the subcutis, three times, but in the kidney, nineteen times. This proportion probably is somewhat low, since sections were not made of the internal organs of all animals and hemorrhages could easily occur which would not show on the surface of the organ. However, sections of the kidney, liver

and spleen were made from a number of selected animals and were stained with Delafield's hematoxylin and eosin, which showed masses of red corpuscles unconfined by the vessel walls. These organs also regularly showed a moderate to pronounced congestion.

Since the completion of this work one of us (B.S.) has observed, under the dietary regimen indicated in table 6, another condition of the nursing young which are suffering from a deficiency of vitamin B; namely, convulsions accompanied by shrills.[2] The young run aimlessly across the cage and bite the screens, injuring their mouths until

Hemorrhagic condition of parietal and occipital bones. 1. One of the young of female 4416 (table 6) in advanced stage of beriberi. The animal showed marked paralysis and chills. It was chloroformed and immediately photographed. Age, 20 days. 2. The last remaining young of female 3980 (table 4) which died, December 11. Autopsy was performed immediately after death and the animal photographed. Age, 20 days. 3. Normal rat; age, 20 days.

they bleed. The paralysis beginning in the posterior quarters is progressive, so that later they can swallow only with great difficulty. More than 100 young in this condition, as well as more than 1,000 young in the paralytic state unaccompanied by spasms, have been saved by administrations of concentrated preparations of vitamin B prepared for this laboratory by the research laboratories of Eli Lilly and Co.

In thirty further necropsies, not previously mentioned in this paper, the hemorrhagic appearance at the junctures of the occipital and parietal bones was found to be 100 per cent.

There are several pertinent considerations regarding the application of this work. The deficiency of cow's milk in vitamin B for lactation has been emphasized in previous publications,[7] in which it was demonstrated that a diet containing as much as 50 per cent dried skimmed milk must be fortified with yeast to furnish enough vitamin B for normal lactation. Recently Macy, Outhouse, Graham, and Long,[8] from their quantitative studies of human milk, concluded that human milk is even more deficient than cow's milk in vitamin B, and they suggest that the milk of the nursing human mother is probably on the borderline as far as vitamin B content is concerned. Guest, Nelson, Parks and Fulmer[9] came to similar conclusions from their studies of the cereals as the only source of vitamin B for fertility and lactation.

Moreover, it is suggested that, while pronounced forms of beriberi or polyneuritis are seldom encountered in this country in the human infant, it is possible that "masked beriberi" occurs more often among infants than has hitherto been recognized. It is easily possible that long before injury to the vascular walls becomes sufficient to lead to their rupture and thus to hemorrhage, the injury has resulted in alterations in the selectivity of these semipermeable membranes which, in turn, naturally would upset the entire metabolic equilibrium. Moreover, work in progress[10] shows that the liver cells of the nursing young in the convulsive state (when the nurslings are still in a reparable condition, so that they respond most readily to vitamin B therapy) show considerable vacuolization and the nuclei are pushed to the side, presenting a typical picture of fatty degeneration of the liver.

We anticipate, however, that in bottle-fed infants deficiencies in vitamin B may be considerably more prevalent among those receiving water as the diluent in the formula than those receiving lactic acid milk which is given in the undiluted form.[11]

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7. Sure, Barnett: Dietary Requirements for Reproduction: III. The Existence of the Reproductive Dietary Complex (Vitamin E) in the Ethereal Extracts of Yellow Corn, Wheat Embryo, and Hemp-Seed, J. Biol. Chem. **62**:371 (Dec.) 1924; IV. Solubility of the Reproductive Dietary Complex (Vitamin E) in Various Organic Solvents, ibid. **63**:211 (March) 1925.

8. Macy, I. C.; Outhouse, J.; Graham, A., and Long, M. L.; Human Milk Studies, J. Biol. Chem. **73**:189 (May) 1927.

9. Guest, A. E.; Nelson, V. E.; Parks, T. B., and Fulmer, E. I.: Diet in Relation to Reproduction and Rearing of Young: II. Am. J. Physiol. **76**:339 (April) 1926.

10. Sure, Barnett; Walker, D. J., and Schilling, S. J.: Unpublished data.

11. Marriott, W. McKim: Preparation of Lactic Acid Mixtures for Infant Feeding, J. A. M. A. **89**:862 (Sept. 10) 1927.

SUMMARY

1. Nursing young suffering with deficiency in vitamin B were found to die with accompanying hemorrhages in the osteogenetic tissues. Hemorrhages were also found in certain of the viscera.

2. Polyneuritic nursing young were found usually to die with their stomachs well distended with curd.

3. The diets on which beriberi or polyneuritis were produced in the nursing young proved entirely satisfactory for maternal welfare and for the growth of nonlactating individuals.

4. It is suggested that deficiencies in vitamin B in infants in this country may be considerably more prevalent than hitherto recognized.

RHEUMATIC NODULES

THEIR INCIDENCE IN RHEUMATIC INFECTIONS *

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It is commonly believed that rheumatic nodules are seen much less frequently in the United States than in England. In order to determine the facts in this matter, all the children showing rheumatic infection of any kind were observed in the Children's Medical Division of Bellevue Hospital for a considerable period. From fall until summer for three years, children with chronic cardiovalvular disease, acute rheumatic fever or chorea were given a systematic examination for the presence of nodules, at intervals of from one to two weeks. Notes were made as to the temperature, clinical course, etc. This study was undertaken on account of the large number of nodules which were observed in the winter and spring of 1923 to 1924. Observers at other hospitals in New York also noted this fact. Apparently that was a high peak of the incidence of rheumatic nodules, for in the three following years, they have been observed with decreasing frequency. Dr. Homer Swift of the Rockefeller Institute said that from 1923 to 1925 he saw more nodules than at any time since he has been observing patients with rheumatic fever. He also stated "It is a well known fact that through certain cycles of years, there is a high incidence, and then a low incidence of the disease." This yearly dissimilarity has also been observed by Coates [1] of England. In the three or four months preceding the writing of his article, he observed in Bristol as many examples of nodules as were seen in the preceding five years. He felt that this is not explained by an increased severity in the type of rheumatic infection. Conditions during this period were apparently similar to those in the United States from 1923 to 1925. Coates felt that in England the striking thing about the nodules is not their rarity, but their extraordinary prevalence. He examined 100 children between the ages of 2 and 12 years at an outpatient department in Bristol and found twenty-three giving a history suggesting a rheumatic infection. Six children had nodules without any rheumatic manifestation at all. Five had nodules before a rheumatic manifestation occurred, and seven had nodules with a rheumatic manifestation. In a later article, Coates

* Received for publication, Jan. 6, 1928.

* From Children's Medical Division and Department of Diseases of Children, College of Physicians and Surgeons, Columbia University.

1. Coates, V.: Brit. M. J. **1**:550 (March 21) 1925.

and Coombs [2] stated that many children with a picture of a latent rheumatic infection, without a definite cardiac lesion, have small subcutaneous nodules which show microscopically the characteristic tissue reaction. This is contrary to the observations at Bellevue Hospital, where in three years only one patient was found who showed nodules without a cardiac lesion. This patient showed acute rheumatic fever only.

This series shows conclusions similar to those of Brennemann [3]: the severity and chronicity of the rheumatic infection are the most important factors in the production of rheumatic nodules, and yet nodules may occur in any patient with rheumatism. They also may be absent in just the patient in whom one would most expect to find them.

The nodules were conspicuous by their absence in patients with acute rheumatic fever with definite joint symptoms, and were most often found in patients with chronic forms with recurrent infections and severely damaged hearts. Several children with chronic cardiovalvular disease who have not shown nodules on their first admission to the hospital have shown them on their second or third admissions.

Brennemann [3] stated that nodules are rarely tender. Examination during this study showed that children often complain of tenderness on having them palpated. Brennemann also stated that they are usually distinctly movable on the deeper structures. Of the nodules examined during the past three years, the majority have been firmly fixed to tendon or fascia. When nodules are present on the joints of the knees or elbows and these joints are flexed, the skin can usually be moved freely over the immovable nodule. Brennemann observed that when a great many nodules are present, some of them are sure to be large. This was confirmed in the study made at Bellevue.

Bronson and Carr [4] found that of twelve children who had apparently completely recovered from attacks of rheumatic fever, only one showed nodules; of nine children with definite cardiac disease, three showed nodules, and of seventeen with severe cardiac disease and decompensation, thirteen had nodules. Of these seventeen, seven died, six of whom had nodules.

From August, 1921 to 1923, Wallace [5] of Chicago, found fifteen, or 12 per cent, of 124 children to have rheumatic nodules at some time during their stay in the hospital. All fifteen showed signs of endo-

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2. Coates, V., and Coombs, C. F.: Arch. Dis. Childhood **1**:183 (Aug.) 1926.

3. Brennemann, J.: Incidence and Significance of Rheumatic Nodules in Children, Am. J. Dis. Child. **18**:179 (Sept.) 1919.

4. Bronson, E., and Carr, E. M.: Am. J. M. Sc. **165**:781, 1923.

5. Wallace, J. H.: Arch. Pediat. **12**:731 (Nov.) 1924. Good bibliographies on the literature may be found in this article and in that of Coates.

carditis. The number of nodules varied from one to fifty at one time in a given child.

Only children showing nodules which were absolutely definite were included in the series at Bellevue; hence, the estimation is conservative.

Table 1 gives an analysis of patients showing nodules for the years 1924 to 1927. It will be seen that patients showing chronic cardiovalvular disease at the time of observation have the highest incidence of nodules. The next highest is chronic cardiovalvular disease with acute rheumatic fever, and the next is chronic cardiovalvular disease with chorea.

In the sixteen patients of the 1924-1925 series, table 2 shows that five had previously been admitted to the hospital one or more times. In the 1923-1924 series, one patient, C. J., showed nodules. As a special examination was not being made at this time, it is not certainly

TABLE 1.—*Incidence of Rheumatic Nodules*

	1924-1925	1925-1926	1926-1927	Total
Total number of admissions observed	74	64	86	224*
Total admissions showing nodules	16	6	6	28†
Percentage of nodules	21%	9%	6%	12%
Chronic cardiovalvular disease alone	6	3	3	12
Chronic cardiovalvular disease with acute rheumatic fever	6	1	3	10
Chronic cardiovalvular disease with chorea	2	2	0	4
Rheumatic fever alone	1	0	0	1
Chronic cardiovalvular disease with acute pericarditis	1	0	0	1

* Total number refers to number of admissions; several of the same children were examined in two successive years.

† Three of the same children appear twice in tables 1, 2 and 3; therefore, the total number of different children showing nodules is twenty-five.

known whether the other patients showed them on their previous admissions. A history of either rheumatic fever or chorea was given by all except one patient with chronic cardiovalvular disease. Many of them had had both. Only one patient did not show involvement of the heart at the time of observation, and had rheumatic fever only. The tonsils were present in eight patients; in two, tonsillectomies were performed during their stay in the hospital. Decayed teeth did not seem to be a factor, as only one child had markedly carious teeth, and only one had an alveolar abscess. There was a family history of rheumatism in four of the children. One child, C. J., had a brother, W. J., who had nodules during 1925-1926. Three children died during the period of observation.

Table 3 shows the six cases in which nodules were found during 1925-1926. Two of them also appear in table 2; one other showed five nodules on a previous admission. All of these children had involvement of the heart. Three had rheumatic fever on admission, one had chorea during his stay in the hospital, and one had chorea just

TABLE 2.—*Data of 1924-1925 Series*

Name	Age, Years	Admission	Family History	Acute Rheumatic Fever	Chorea	Chronic Cardiovalvular Disease	Tonsils	Other Symptoms	Usual Temperature Range	Maximum Number of Nodules and Size*	Weeks Patient Was Observed	Sites of Nodules	Discharge; Death
C. J.	11	Two previous admissions; nodules present last admission, 10/3/24	Brother has C. C. V. D. grandmother "rheumatic"	At 2 years	None	Mitral stenosis and regurgitation; hypertrophy, class III	Removed	Edema and ascites	98.6 to 101 or 102	10, mostly medium, a few large	20	Elbows, knees	Died, 3/15/25
C. B.	11	11/20/24	Negative	1 year ago and P. I.†	None	Mitral stenosis and regurgitation; hypertrophy, class III	2 plus	Edema; ascites; liver and spleen palpable; abscessed tooth	99 to 103	1, medium	30	Knee	7/1/25, not located
A. B.	11½	11/—/24	Negative	3½ years ago, 1 year ago	2 years ago, 1 year ago	Mitral stenosis and regurgitation; hypertrophy, class III	Removed	Liver palpable; edema of legs	98.6 to 102	4, mostly medium	4	Elbows	Died, 12/17/24
H. S.	9	11/29/24, 3/9/25	Negative	P. I.	None	Negative, class V	2 plus; removed, 3/25	Pain in right knee	98.6	3, medium and small	3 and 2	Elbow, scalp	4/25, in good condition
A. M.	10	12/4/24	Negative	"Every year"	None	Mitral stenosis and regurgitation; aortic regurgitation; hypertrophy, class III	Removed Tonsil tags left	Liver palpable; pyelitis; lobar pneumonia	98 to 104	2, medium and small	18	Elbow, wrist	Died, 5/2/25
H. G.	7	12/6/24	Negative	None	None	Mitral stenosis and regurgitation; friction rub, class III	Removed	Fluid in pleural cavities; two carious teeth	98.6 to 103	15, mostly medium, a few large and small	5	Elbows, ankles	Died, 1/11/25
M. G.	9	12/15/24, 4/8/25	Negative	9 months ago	None	Mitral stenosis and regurgitation; hypertrophy, class III	3 plus	Edema; palpable liver	99 to 102	12, equally medium and small; a few large	13	Elbows, knees, malleolus	2/25, not located

R. G.	10	One previous admission, 1/23/25	Negative	P. I.	None	Mitral stenosis and regurgitation; acute pericarditis previously, class III	1 plus	Edema of feet and ankles; liver palpable; fluid in right side of chest	99 to 100	1, medium	10 days	Elbow	2/25, not located
D. P.	7	3/20/25	Negative	None	Two attacks and P. I.	Mitral stenosis and regurgitation; hypertrophy, class II A	3 plus	None	99 to 101.5	4, mostly large	4	None on admission; later, knees, malleolus, hands, scalp	6/26/25, not located
M. J.	11	3/21/25	Negative	P. I.	None	Mitral regurgitation, class III	Removed	Knees and ankles painful	98.6 to 101.2	1, medium	4	Malleolus	Died, 4/25
M. S.	6	4/6/25	Negative	1 year ago and P. I.	None	Mitral stenosis and regurgitation, class II B	2 plus	Spleen palpable	98 to 103	5, medium and small	9	Elbows, knees, hands, malleolus	8/5/25, not located
V. C.	9	4/13/25	M. F. and one other child had "rheumatism"	Two previous attacks; present one of 4 months' duration	One attack	Mitral stenosis and regurgitation; aortic regurgitation, class III	Removed	None	99	5, mostly medium	6 days	Elbow	Died, 4/19/25
O. C.	7¾	4/18/25	Negative	P. I.	None	Mitral stenosis and regurgitation, class III	2 plus, removed	Swelling of legs and ankles; palpable liver; erythema multiforme	98 to 102	14, mostly medium, a few small	7	Elbows, knees, spine	6/25, in hospital October, 1927
B. H.	10	4/27/25	M. had "rheumatism"	P. I.	None	Mitral stenosis and regurgitation; hypertrophy, class II B	4 plus	None	98 to 102	6, equally medium and small	7	Elbows, knees, hands, malleolus	8/25/25, not located
E. H.	8	5/14/25	M. had chorea and C. C. V. D.	6 months ago	Slight	Mitral stenosis and regurgitation; hypertrophy; pericardial effusion, class III	1 plus	None	98 to 100	29, mostly medium, a few large and small	1	Elbows, knees, malleolus, hands, scalp, scapula	5/20/25, not located
D. A.	7¼	5/20/25	Negative	P. I.	None	Mitral regurgitation; hypertrophy, class II A	Removed	None	98 to 100.8	38, mostly medium, a few large	4	Wrists, elbows, knees, malleolus, feet, hands	7/23/25, not located

* Size: large, medium and small.
† In this table and in table 3, P. I. indicates present illness.

before admission. In four children, the tonsils were still present on admission, and in two the tonsils were removed during their stay. Carious teeth were not a factor. There was a significant family history in two cases. One child died.

Table 4 gives the data for the six cases in which nodules were found during 1926-1927. Three of the children had been admitted to the hospital previously. Two patients, G. H. and W. H., are mentioned in table 3. All six showed involvement of the heart; two had not had either rheumatic fever or chorea. One had had rheumatic fever. Two had had chorea. Two had rheumatic fever on admission. In two the tonsils were still present. Carious teeth were not a factor. A family history of rheumatism was present in one case. One patient died of pneumococcus septicemia.

Figure 1

Figure 2

Fig. 1.—Appearance of nodules on elbow.

Fig. 2.—Appearance of nodules on hand.

Table 5 shows an analysis of cases in which nodules were not present. In the three year series, there were forty-two patients with chronic cardiovalvular disease without nodules, in comparison with twelve who had nodules; twenty-four patients with chronic cardiovalvular disease and chorea without nodules, in comparison with four who had nodules; twenty-eight patients with chronic cardiovalvular disease with rheumatic fever, in comparison with two who had nodules; fifteen patients with rheumatic fever only without nodules, in comparison with one who had nodules, and three patients with acute pericarditis, in comparison with one who had nodules (this patient also had chronic cardiovalvular disease).

There seem not to be any laws that definitely determine which patients with cardiac involvement will develop rheumatic nodules. The

TABLE 3.—*Data of 1925-1926 Series*

Name	Age, Years	Admission	Family History	Acute Rheumatic Fever	Chorea	Chronic Cardiovalvular Disease	Tonsils	Other Symptoms	Usual Temperature Range	Maximum Number of Nodules and Size	Weeks Patient Was Observed	Sites of Nodules	Discharge: Death
W. J.	5	Previous admission, 7/8/25	Brother died of chronic cardiovalvular disease in 1925 (See C. J., 1924-1925)	P. I.	None	Mitral stenosis and regurgitation; hypertrophy, class III	Removed 2 years ago	Pericardial friction rub; edema	98 to 103	11, mostly small	17	Elbows, scalp	Discharge, 4/26; died later
G. H.	5	9/19/25	Negative	P. I.	None	Mitral stenosis and regurgitation; hypertrophy, class II A	2 plus; removed 11/25	None	100 to 101	1, small	2	Many seen on hands, knees, feet and scalp previous to study	11/25; in good condition
M. S.	6	8/27/25	Negative	On previous admissions	None	Mitral regurgitation; hypertrophy, class II B	1 plus; removed 10/25	Palpable spleen	98 to 101.5	2, large	6	Elbows	12/25; not located
W. H. (see 1926-1927)	5	10/16/25	Negative	None	None	Mitral regurgitation; hypertrophy, class II B	Removed at 4 years	Liver palpable	98 to 100.4	6, medium and large	17	Elbows, knees, scalp	3/26; in hospital, Oct., 1927
F. G.	9	1/14/26	Negative	P. I.	None	Mitral regurgitation; aortic regurgitation, class III	3 plus	Swelling and redness of left ankle; tenderness of knees and wrists; pericardial friction rub	98.6 to 105	4, mostly medium	16	Knees	5/20/26; not located
G. O.	8	4/7/26, 8/24/26	Sister had chorea and was in hospital at same time	None	Onset of P. I. with chorea	Mitral regurgitation, class II B	2 plus	None	98 to 100	8, mostly large and medium	8	Elbows, scalp	7/14/26; 9/12/26; not located

type of patient with chronic cardiovalvular disease familiar in wards admitting children with chronic forms of the disease—the child who has been in the hospital several times previously; who is pale, thin and dyspneic, and has often had cough, and who has an acute exacerbation of the rheumatic infection with a temperature ranging from normal to 101 or 102—is the one who is most apt to show nodules. Often they do not appear at the first admission or during the acute exacerbation. They may begin to appear after the temperature has dropped and the child is clinically improved. The number of nodules is extremely variable. In this series, they varied from one to thirty-eight at one observation. The majority of the ones of moderate size last for from five to six

Fig. 3.—Appearance of nodules on the scalp.

weeks, whereas the large ones may last from eight to nine months. S. O. (1926-1927 series), who had first shown nodules in the summer of 1926, still showed them in May, 1927. The small nodules may disappear within a week. In a patient who shows many nodules from the start, new crops keep appearing. The tendency of most of the nodules is gradually to grow smaller and finally to disappear.

PATHOLOGY

Barlow and Warner [6] gave the first good account of subcutaneous nodules, and their conclusion was that "such nodules belong strictly to

6. Barlow, T., and Warner, F.: Tr. Internat. Med. Congress, London, 1881, vol. 4, p. 116.

the fibrous tissues, and in nature are probably homologous with the inflammatory exudate which forms the basis of a vegetation in a cardiac valve."

Coates and Coombs [2] concluded:

the center of the lesion is a thrombosis, around which is a zone of extraordinarily rich and exuberant proliferation of fibrous and endothelial cells; these last throwing off not only detached uninucleate cells, but also new capillary buds in great numbers, and forming, possibly as an early phase of this budding, the

Fig. 4.—Appearance of nodules on the spine.

multinucleate cells that are so striking a feature of the rheumatic reaction. These characters, the thrombotic center, and the endothelial periphery, stamp the node as a vascular lesion.

Coates and Coombs showed photomicrographs of nodules from patients with endocarditis, rheumatoid arthritis and chronic cardiovalvular disease, and a patient with cardiac hypertrophy without a valvular lesion, who showed a similar tissue reaction.

In his article on the Pathogenesis of Rheumatic Fever, Homer Swift [7] said,

7. Swift, Homer F.: J. Exper. Med. **39**:497, 1924.

TABLE 4.—*Data of 1926-1927 Series*

Name	Age, Years	Admission	Family History	Acute Rheumatic Fever	Chorea	Chronic Cardiovalvular Disease	Tonsils	Other Symptoms	Usual Temperature Range	Maximum Number of Nodules and Size	Weeks Patient Was Observed	Sites of Nodules	Discharge: Death
S. O.	9	Previous admission, 7/23/26	Negative	1 year ago, also on admission	Several attacks	Mitral stenosis and regurgitation; aortic regurgitation; hypertrophy, class II B	Removed at 8 years	None	From subnormal to 101; occasionally 102, 103 or 104	25, mostly small and medium, many large	28	Elbows, knees, hands, feet	6/10/27; in hospital, Oct., 1927
T. K.	9	9/27/26	Mother has "heart trouble"	Pains in extremities	None	Mitral stenosis and regurgitation; hypertrophy, class II B	Removed at 8 years	None	From subnormal to 101; occasionally 102 to 103	8, mostly small; a few medium and large	7	Elbows, knees	12/23/26; not located
J. R.	11	10/27/26	Negative	None	2 years ago	For two years mitral stenosis and regurgitation; hypertrophy, class III	1 plus	None	From subnormal to 102	1, medium	4	Elbow	Died, 11/30/26, of pneumococcus septicemia
W. H.	6	Several previous admissions; 1/7/27	Negative	None	None	Mitral regurgitation; hypertrophy, class II B	Removed at 4 years	None	From 98 to 102	19, equally small, medium and large	17	Elbows, knees, hands, feet	6/27; in hospital, Oct., 1927
H. K.	5	1/29/27	Negative	None	None	Mitral stenosis and regurgitation; hypertrophy, class II B	2 plus	None	From subnormal to 100.5	2, medium	2	Elbows, scalp	2/11/27, not located
G. H.	6	4/29/27	Negative	1½ years ago in hospital with acute rheumatic fever pains in the joints 3 months ago, also 3 days before admission	None	Mitral and aortic regurgitation, class II A	Removed at 5 years	None	From subnormal to 100.5; 102 on admission	19, medium and small; a few large	3	Elbows, knees, malleolus, hands, feet	6/10/27, in good condition

For many years English clinicians have called attention to the frequent occurrence of fibroid nodules in the subcutaneous tissue of rheumatic children. Anatomically they are found in the deep fascia over bony prominences and in tendon sheaths and tendons. The essential histological picture is similar to that seen in the Aschoff body. In close apposition to areas of cellular proliferation there is tissue destruction varying in size from small submiliary areas to long strands of hyaline necrosis affecting connective tissue fibers; combined with necrosis are deposits of fibrin. Surrounding these destroyed foci are found numerous cells similar in appearance and staining reaction to the type of cells found in Aschoff bodies, multinuclear giant cells are also present. In nodules it is not difficult to demonstrate these endotheliod cells arising from perivascular spaces as well as from the vascular endothelium. In fact, the participation of the blood vessels in the general response is one of the most marked features of the subcutaneous nodules. Many capillaries are seen in which the swollen endothelium has practically obliterated the lumen; in the arterioles the proliferation of the endothelium at times takes the form of a crescent-shaped mass

TABLE 5.—*Analysis of Patients Not Having Nodules*

	1924-1925	1925-1926	1926-1927	Total
Chorea alone	20	13	30	63
Chorea with rheumatic fever	1	1	0	2
Chorea with definite chronic cardiovalvular disease	7	5	12	24
Chorea with "possible" cardiac involvement	2	10	0	12
Chronic cardiovalvular disease alone	13	11	18	42
Chronic cardiovalvular disease with rheumatic fever	5	9	14	28
Chronic cardiovalvular disease with acute pericarditis	0	0	1	1
Rheumatic fever alone	7	3	5	15
Rheumatic fever with "possible" cardiac involvement	0	5	0	5
Rheumatic fever with pericarditis	0	1	0	1
Acute pericarditis	3	0	0	3
Totals	58	58	80	196

of cells, appreciably narrowing the vessel. Still other small arteries are seen obliterated by thrombi; in others the media is involved, and surrounding many of the smaller vessels there can often be seen collections of endothelioid cells evidently compressing the walls. A participation of fibroblasts arising from the connective tissue is easy to demonstrate. A few polymorphonuclear cells and lymphocytes invade the diseased tissue and foci of edema are demonstrable. While, grossly, these nodules vary in size from 0.5 to 5.0 or 10.0 mm. it is evident upon microscopic examination that the larger nodules are composed of a conglomeration of submiliary nodules. The pathological unity of the myocardial and subcutaneous lesions is, therefore, easily comprehensible.

According to Dr. Douglas Symmers,[8]

The occurrence of rheumatic nodules in anatomical relationship with aponeurotic and related structures, suggests that these bodies are of fibrous tissue origin and their histology would seem to substantiate this view. Microscopic examination of them shows more or less well circumscribed collections of cells with oblong or plump, moderately chromatic nuclei and a cytoplasm which presents

8. Symmers, Douglas: Unpublished communication.

a collagenous appearance. At the periphery of these cell collections are numbers of endothelial slits, representing blood vessels or lymph spaces. Many of the nodules exhibit an histology not more complex than that just outlined, but in some of them multinucleated giant cells are to be made out in apposition to hyalinized remains of collagenous fibrils—a foreign body reaction. In still other instances, areas of necrosis are to be made out, sometimes to an excessive degree. Thus, I see no histological relationship between the rheumatic nodules

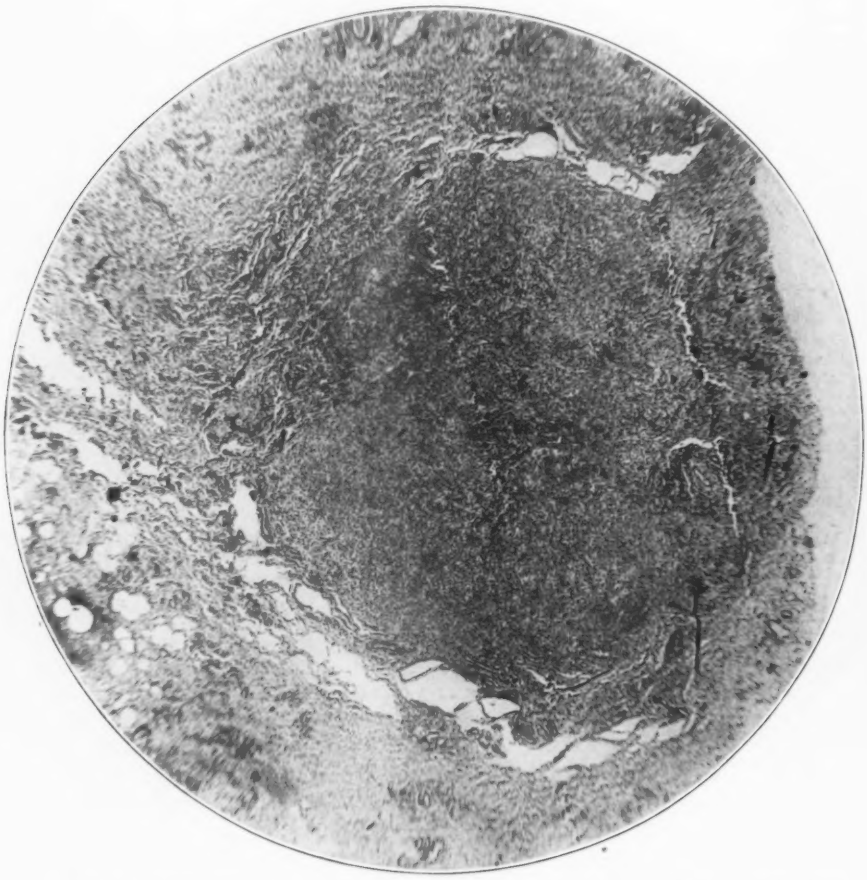

Fig. 5.—Appearance of nodule under a low power lens. This nodule was 2 mm. in diameter.

and the so-called Aschoff bodies which are encountered in the myocardium in certain rheumatic conditions. In the latter structures, the heart muscle fibers themselves appear to suffer local damage, followed by an attempt to regenerate, with subsequent formation of multinucleated giant cells, due to division of nuclei and failure of the sarcolemma to divide. The Aschoff bodies, I believe, contrary to most opinion, have no specific relationship to perivascular structures. Their histology bears a certain resemblance, however, to the changes seen in Zenker's degeneration of the recti muscles in enteric fever and other infective conditions, and in experimental attempts to regenerate voluntary muscle tissue.

Fig. 6.—Appearance of nodule under a high power lens, showing collagenous fibrils with moderate nuclear proliferation and a central multinucleated giant cell.

SUMMARY

Two hundred and twenty-four patients showing rheumatic infections were observed during the fall, winter and spring of the years 1924 to 1927. Twenty-five children showed nodules, three of them in more than one attack. They appear most frequently in patients with severe cardiac involvement and point to a poor prognosis. There were eight deaths in twenty-five patients under observation.

It seems fair to conclude from the unrecorded and recorded observations that the incidence of nodules varies in different years, and that it is not a geographic question.

ROENTGENOGRAPHIC CHANGES IN THE THORAX OF NORMAL NEW-BORN BABIES

A DAILY ROENTGENOGRAPHIC STUDY OF TWENTY-FIVE NORMAL BABIES DURING THE FIRST FOURTEEN DAYS OF LIFE *

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BROOKLYN

The need for fuller knowledge of the roentgenographic changes that occur in the thorax of normal new-born infants during the first two weeks of life has been keenly felt by clinicians. This lack of information was brought forcibly home to us by the critical illness of an infant, 8 days old, who was seen in the nursery of the obstetric department of the Long Island College Hospital. The clinical picture was confusing, and suggested the possibility of pneumonia or intracranial injury. A roentgenogram of the thorax showed diffuse pulmonary mottling, particularly peribronchial, which extended well toward the parenchyma of the lung. There were numerous pea-sized or slightly larger opaque shadows about the hilum of the right lung. The resemblance to roentgenograms considered typical of bronchopneumonic consolidation of later infancy was striking.

In order to decide the importance of these shadows, it seemed essential to know whether roentgenograms of the thorax of normal infants 8 days old show similar shadows.

Review of the literature disclosed but two references that deal to some extent with these particular questions. The first was a preliminary report by De Buys and Samuel,[1] which described the films of the thorax of fifty-six new-born infants. Their cases were unselected, and the roentgenograms were taken only on the day of birth. These authors were most impressed by the variation in the contour of the heart shadow. They did not undertake the description of the lung fields, and emphasized the necessity for further study. The second

* Received for publication, Jan. 3, 1927.

* From the Department of Pediatrics of the Long Island College Hospital.

1. De Buys, L. R., and Samuel, E. C.: Shadows in Thorax of the Newly Born, Am. J. Dis. Child. **24**:397 (Nov.) 1922.

Fig. 1.—Frame for making thorax roentgenograms of infants. An infant is asleep on the frame.

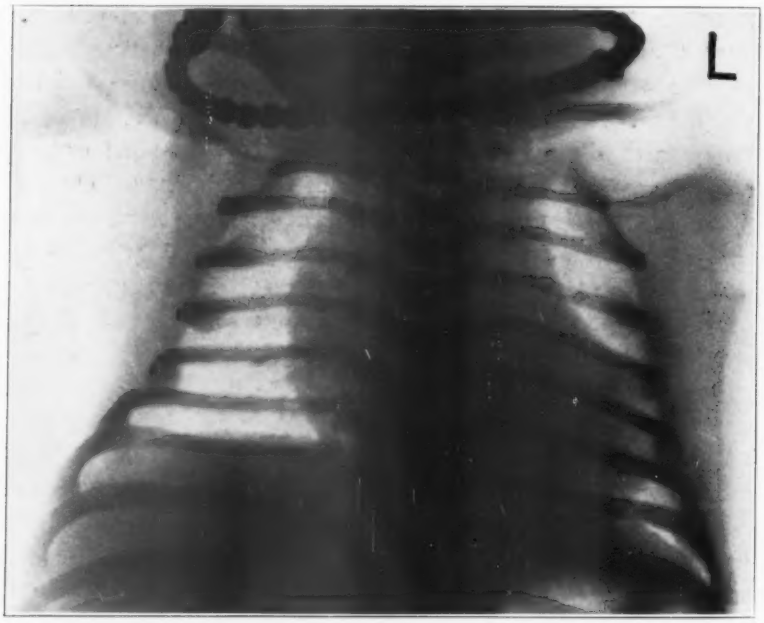

Fig. 2.—Rea, first day film; linear pulmonary markings are seen. A definite interlobar pleural line between right upper and middle lobes is noted. The cardiac shadow is much larger than on the second day. The circle at the top represents beads about the infant's neck.

reference included studies by Wasson [2] which were made more from the point of view of the roentgenologist. His papers described the roentgenographic observations of the thorax of normal infants shortly after birth, after twenty-four hours, after forty-eight hours and again on the fourteenth day. He clearly showed that uniform and satisfactory roentgenograms of the thorax of new-born infants could regularly be taken. He also described postmortem observations which indicated that the shadows seen by him while the patient was living

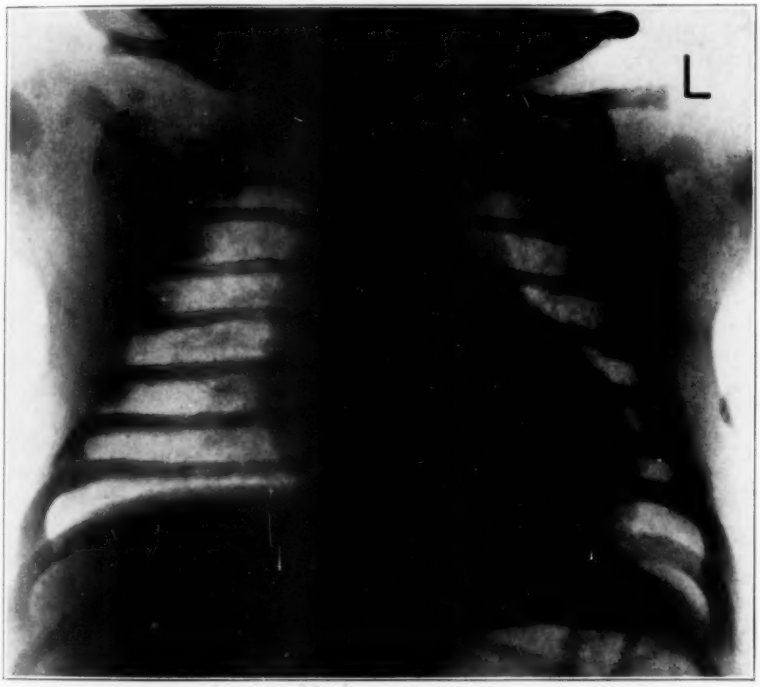

Fig. 3.—Rea, second day film; little change in linear markings is seen. The interlobar pleural line is less conspicuous. The cardiac shadow is relatively smaller than on the first day, but larger than on the third and subsequent days.

had been correctly identified. Helpful points were made and will be mentioned later in connection with certain of our roentgenograms that were taken on similar days. The important question left unsettled by his series was whether significant changes did or did not take place

2. Wasson, W. W.: A Roentgenographic Study of the Infant Chest as seen at Birth, J. A. M. A. **83**:1240 (Oct. 18) 1924; Radiography of the Infant Chest with Special Reference to the "Progression of the Chest and the Determination of the Normal," Radiology **5**:365 (Nov.) 1925.

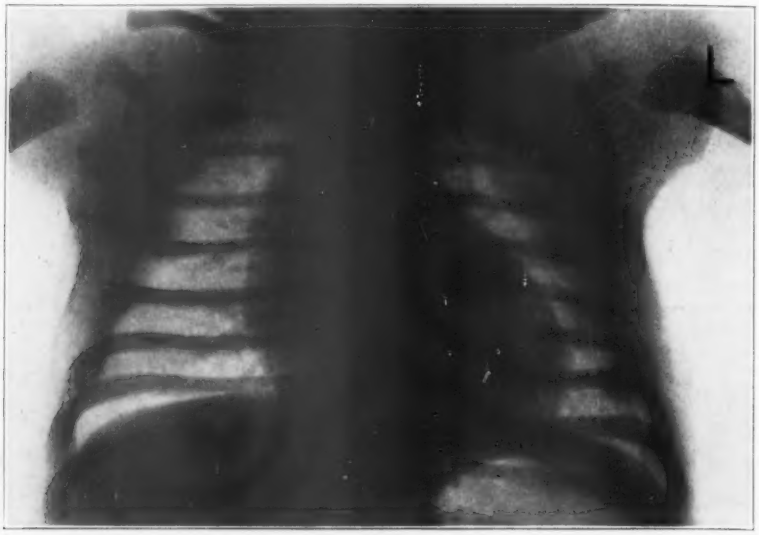

Fig. 4.—Rea, third day film; interlobar pleural line is very faint. No other noteworthy change is seen.

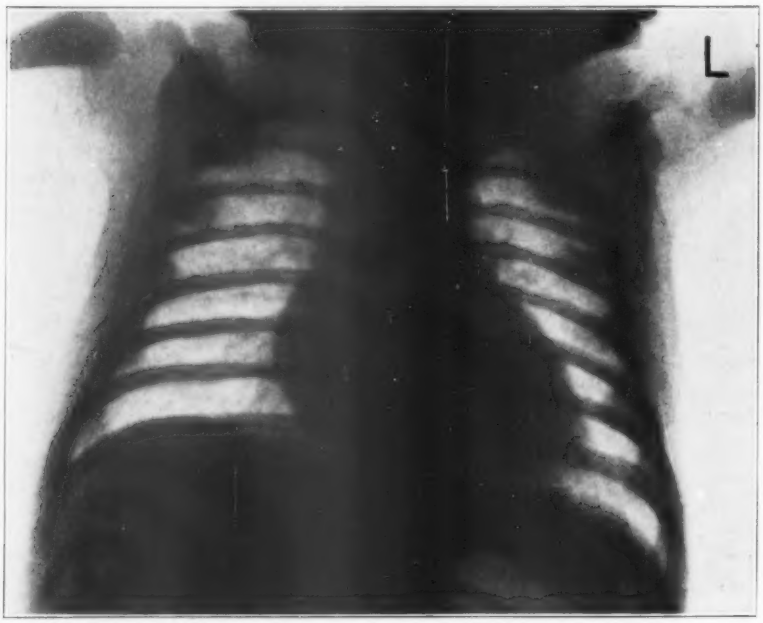

Fig. 5.—Rea, fourth day film; linear pulmonary markings are well seen. The interlobar pleural line is visible. The cardiac shadow is definitely smaller than on any previous day.

from the forty-eighth hour to the fourteenth day. Furthermore, detailed study of the pulmonary fields with particular reference to the exclusion of pneumonia was not undertaken.

EXPERIMENTAL WORK

With these particular points in mind, we made a combined radiographic and clinical study of twenty-five normal new-born infants.

The infants were of average weight (between 2,700 and 4,760 Gm.), and did not have any physical defects that we could find. Complete physical examination was made each day of the entire period with particular attention to the question of abnormal pulmonary or cardiac

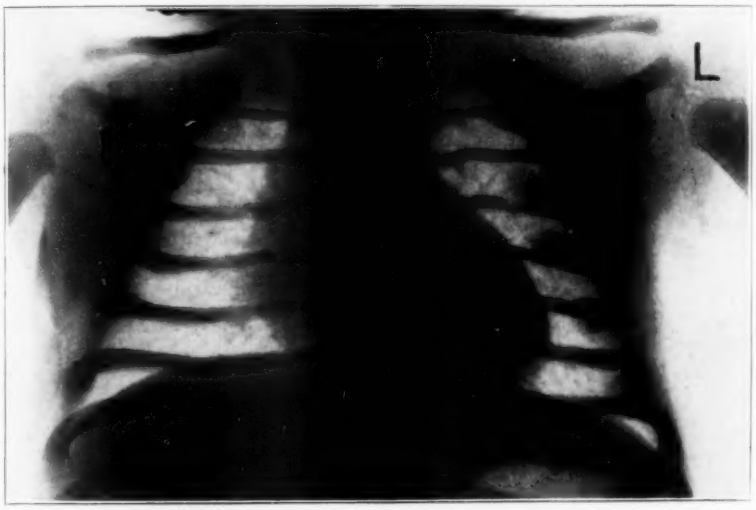

Fig. 6.—Rea, fifth day film; linear pulmonary markings are prominent; the interlobar pleural line, faint.

signs. If the infant developed fever, lost an unusual amount of weight, or in any way differed from the average, the roentgenograms were excluded from the series.

The mothers had been followed by the prenatal clinic of the Long Island College Hospital and were known to have had normal pregnancies. All had negative Wassermann tests of the blood. They were delivered in the hospital after uncomplicated labor of usual duration. None of the deliveries was a breech delivery. Morbidity did not occur during their stay in the hospital. The first twelve babies were born in the fall and winter of 1925; the remainder were born in the spring and summer of 1926

It seemed to us that adherence to these criteria permits this group to be considered a control series.

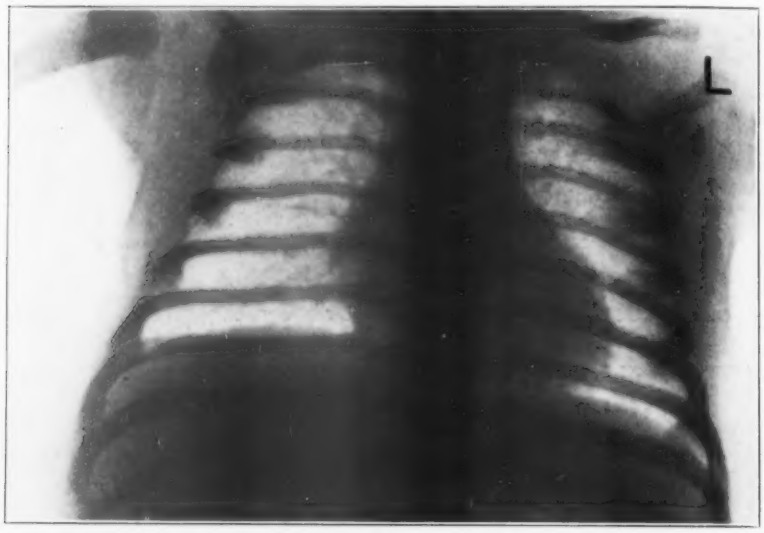

Fig. 7.—Rea, sixth day film; little change except that interlobar pleural line is again plainly visible.

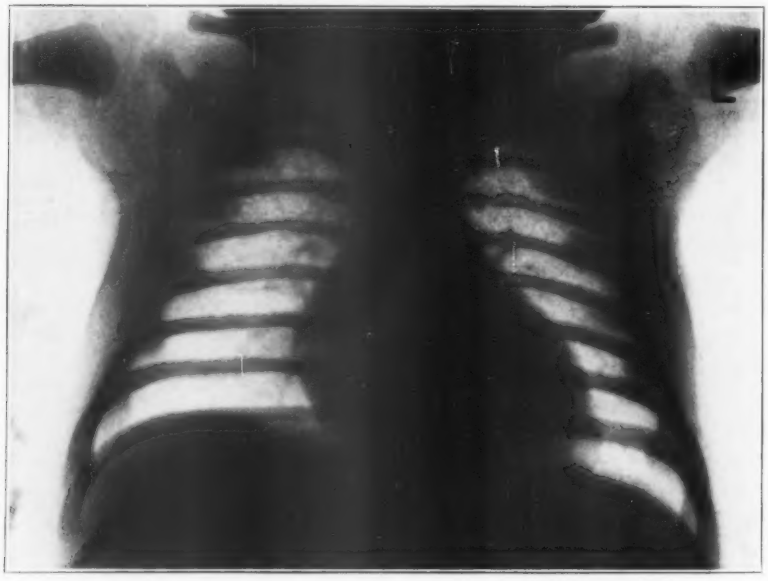

Fig. 8.—Rea, seventh day film; linear pulmonary markings are especially dense about both hilum regions. The interlobar pleural line is faintly seen.

TECHNIC

From the standpoint of roentgen-ray technic, considerable difficulty was experienced in keeping the infants quiet and in making direct anteroposterior exposures. The infants always had the tendency to turn their heads from side to side, which caused the thorax to become slightly twisted. The result was an oblique position. We therefore built a small frame composed of a baseboard of five-ply veneer which measured 24 inches in length and 8 inches in breadth. This base board was supported on each end by blocks 1 inch thick.

These blocks permitted a cassette to be placed beneath the baseboard. Small pieces of the veneer board, measuring 8 inches long and 2 inches wide, were

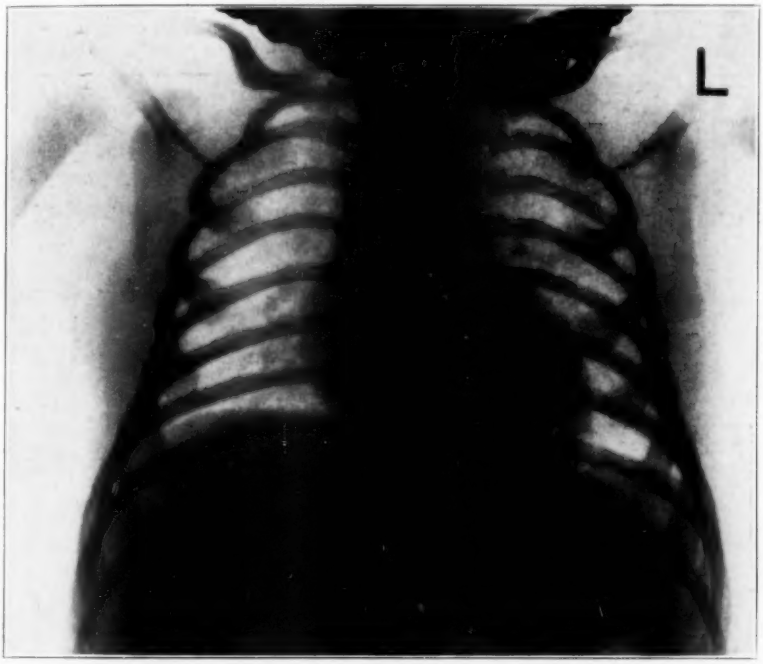

Fig. 9.—Rea, eighth day film; no noteworthy change is noted.

attached on each side of the baseboard 6 inches from one end; these were used as supports for the arms. Side boards were attached on either side of the arm strips to prevent side movements. After the baby was placed in the frame, the spaces between the head and the side boards and spaces between the abdomen and the side boards were packed with folded towels in order to prevent slight movements. The arms were strapped to the arm support. One strap was placed across the legs at the knees, and, if the baby was unusually active, a strap was placed across the abdomen. Occasionally it was found necessary to place a strap across the forehead. By use of this frame, satisfactory roentgenograms could usually be made on the first trial.

The factors used for the exposures were: 5 inch spark gap, 30 milliamperes, 26 inch distance and exposure for one twentieth of a second. Double screens were used.

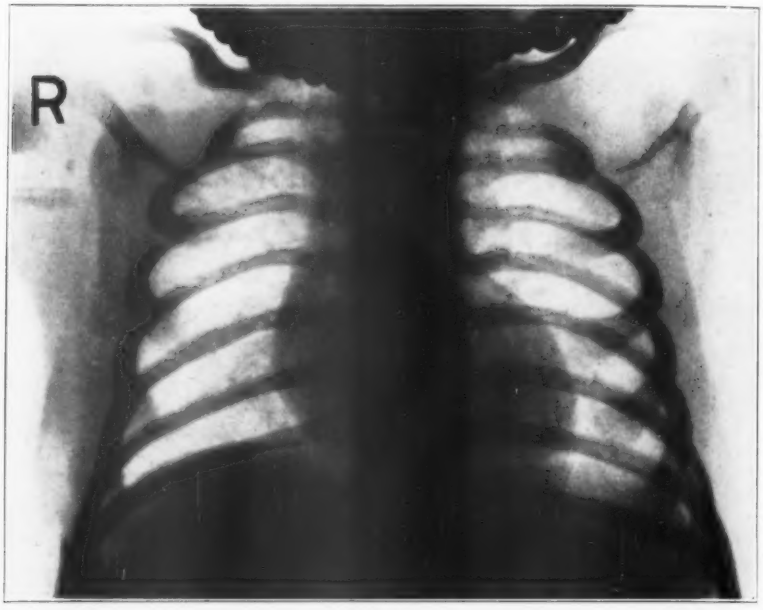

Fig. 10.—Rea, ninth day film; interlobar pleural line is clearly visible. No other noteworthy change is noted.

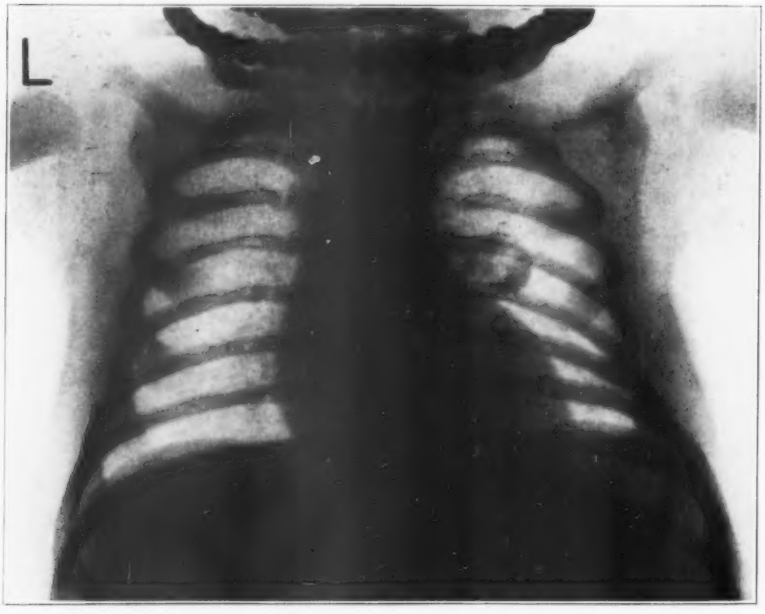

Fig. 11.—Rea, tenth day film; no noteworthy changes are noted.

An attempt was made to take the roentgenograms at the height of inspiration. If the child was not crying, the respirations were watched for several seconds and the exposure made as nearly as possible at full inspiration. If the child was crying, the exposure was made immediately after the beginning of expiration.

OBSERVATIONS

Pulmonary Fields.—Our chief interest lay in the roentgenographic observations in the pulmonary fields. The most striking observation was the almost invariable, well marked definition of the bronchial

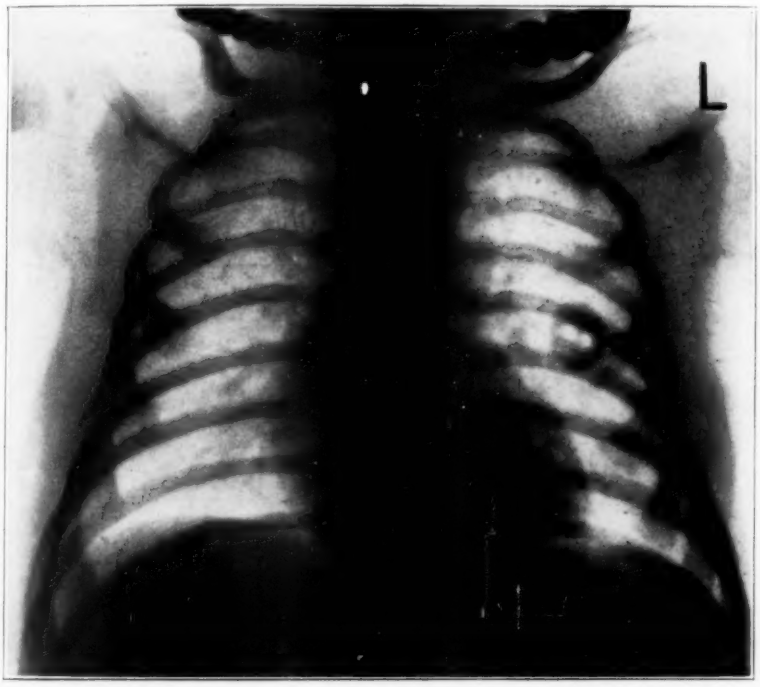

Fig. 12.—Rea, eleventh day film; no noteworthy changes are noted.

trees which extended well toward the parenchyma of the lung. There were frequently considerable mottling and peribronchial thickening to an extent which is often interpreted as characteristic of pneumonia. This had been commented on by Wasson in his description of the pulmonary fields of infants for the first two days and the fourteenth day. When there was variation in the intensity of the linear shadows, it was found to be much more distinct on the films of the first and second days (fig. 6). This was true in ten of our twenty-five patients. The linear markings persisted throughout the series.

It was most interesting to note that in eleven of the twenty-five patients the interlobar pleura between the right upper and middle lobes

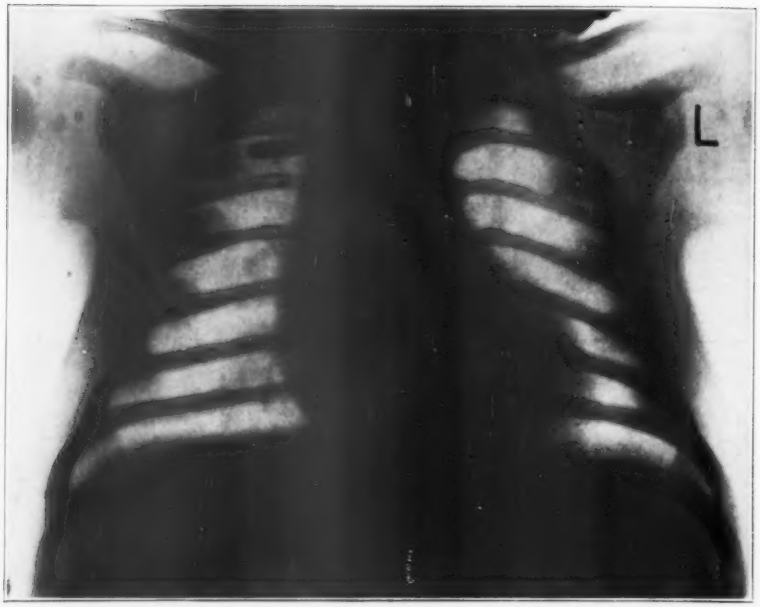

Fig. 13.—Rea, twelth day film; no noteworthy changes are noted.

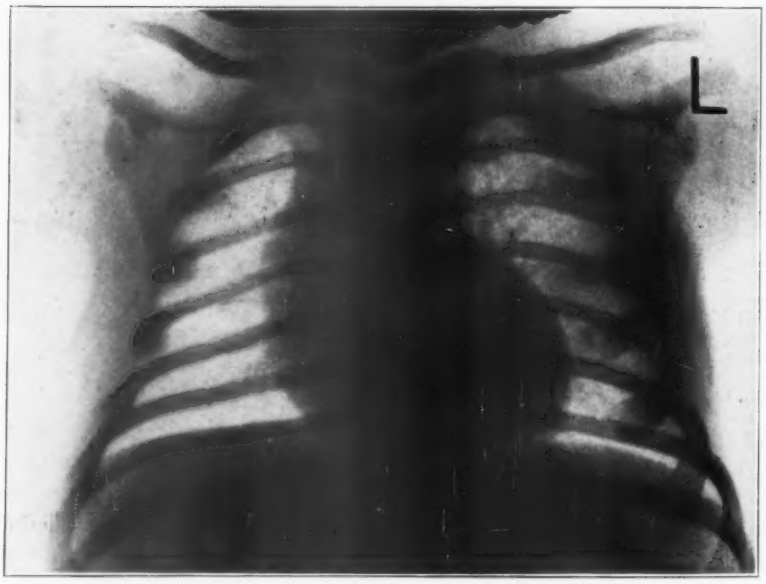

Fig. 14.—Rea, thirteenth day film; linear markings are well seen. The interlobar pleural line is well seen. Contrast the width of the upper mediastinal shadow in this film with that of the day previous and the day following. The difference is due to the position of the diaphragm. This picture was taken in partial expiration.

was sufficiently thickened to cast a definite shadow. This shadow, when present, persisted throughout the series with changes in intensity which depended on the relationship between the plane of the fissure and the ray.

There was only one case which showed radiographic evidence suggestive of atelectasis, and this evidence had disappeared after twenty-four hours. Another apparently normal infant showed an area of density in the left lung field which was hemispherical, about 1 cm. long and 0.5 cm. wide, and which extended upward into the left upper lobar lung field. The shadow persisted for twelve days in the same intensity and in

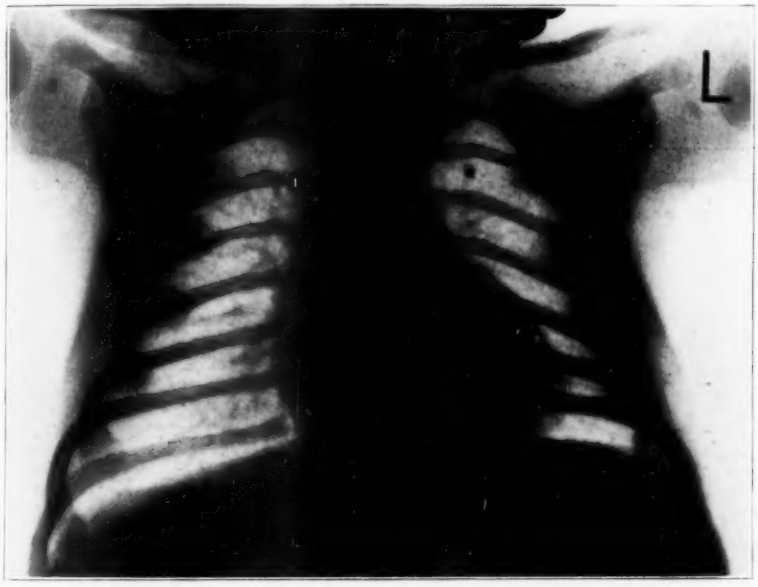

Fig. 15.—Rea, fourteenth day film; no noteworthy changes are noted.

similar dimensions. It resembled the shadow seen in adults that is believed to be cast by lymph nodes.

Heart Shadow.—It was clear from the outset that accurate measurement of the changes in size of the heart was impossible. It was likewise impossible to view this series of roentgenograms without being impressed by the relative difference in the size of the cardiac and vessel shadows after the second day in at least half of the cases. The size of the heart seemed almost not to vary after the second day.

Patient Ser., an apparently normal baby, had so huge a cardiac shadow on the first day that other thoracic shadows were practically obliterated (fig. 16). The shadow of the heart was globular and

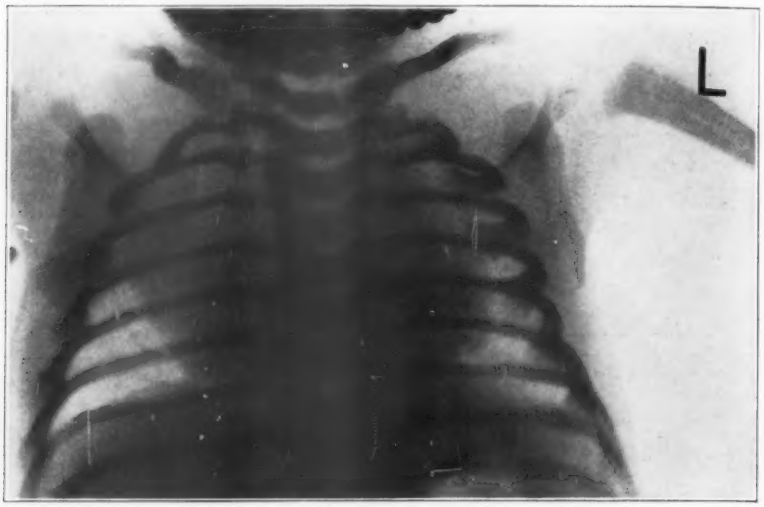

Fig. 16.—Baby Ser., first day film; the huge cardiac shadow almost obliterates other thoracic shadows. This baby had no untoward symptoms. Physical observations suggestive of this situation were not elicited.

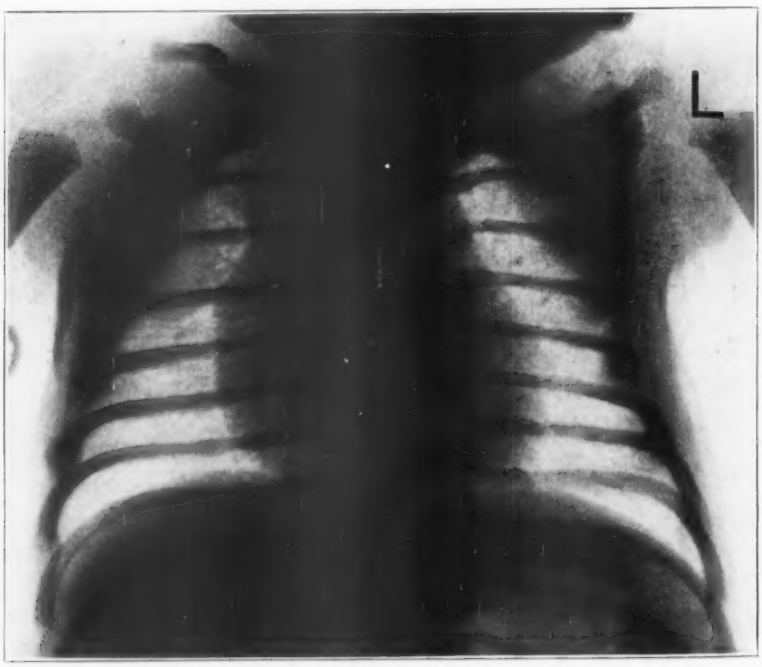

Fig. 17.—Baby Ser., second day film; the cardiac shadow is very much diminished. The baby apparently is perfectly normal.

extended almost to the wall of the chest and the third rib level in each axillary line. On the second day, the shadow had diminished to the average size, but showed a peculiar outward angulation of the upper portion of the right border. Following this day, the angulation had disappeared, and the heart was perhaps 10 per cent smaller than on the second day and much smaller than on the first day. At no time during the stay in the hospital was there cyanosis, or other untoward symptoms. Cardiac murmurs were not heard at any time.

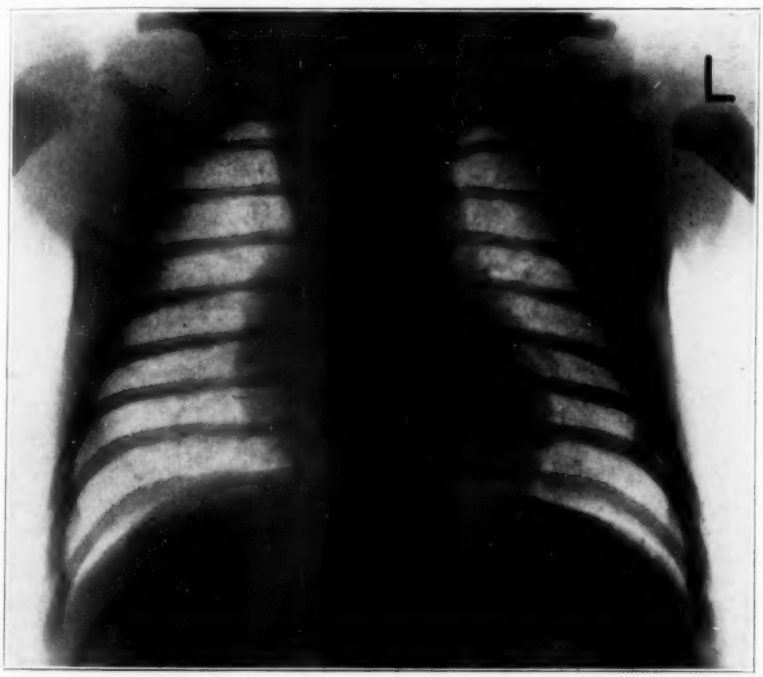

Fig. 18.—Baby Ser., third day film; the cardiac shadow is still further diminished. This shadow is about the average third day shadow for our series. The baby is apparently perfectly normal.

In great contrast was the observation of a much smaller heart than the average in the roentgenograms of patient Sob. This was true of every film, and little variation was noted with each day.

The variation in cardiac contour was individual, and was marked throughout the series.

Mediastinum.—One of the most helpful points from a practical standpoint was found during the observation of the changes in the width of the upper part of the mediastinum, as viewed in the com-

plete daily series. This was particularly true in five instances in which the upper part of the mediastinum cast shadows of average width for a number of days, and on a single day a very wide one, such as had been considered diagnostic of thymic enlargement. On the following day, the shadow was again of average width. The roentgenograms which showed wide upper mediastinal shadows had been taken during or at the end of expiration. This was proved by the lesser count of intercostal spaces above the diaphragmatic shadow. These observations are in agreement with the earlier ones of Gerstenberger.[3] He clearly

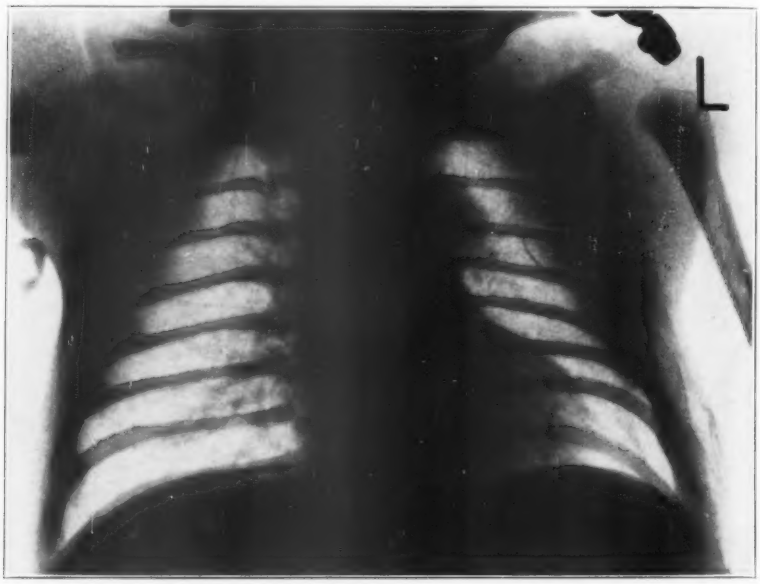

Fig. 19.—Baby Noe., first film; note peculiar hemispherical shadow in the region of the left apex which, when observed in roentgenograms of adults, has been interpreted as cast by lymph nodes. The infant was apparently normal. Usual prominent linear markings and interlobar shadow are seen.

showed that it is dangerous to diagnose enlargement of the thymus from a single film which has perhaps been taken during expiration.

In only one patient did we find a persistently wide shadow which did not vary with respiration. This infant did not have any symptoms during its stay in the hospital, but has not been observed since it was discharged.

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3. Gerstenberger, H. J.: The Factor of the Position of the Diaphragm in Roentgen-Ray Diagnosis of Enlarged Thymus, Tr. Am. Pediat. Soc. **32**:160 (June) 1920.

TABLE 1.—*Roentgenographic Observations in Two Groups of Infants*

First Group, Sept., 1925-Jan., 1926

Name	Birth Weight Gm.	Pulmonary Fields	Cardiac Shadow	Mediastinum
Dol.	2,700	Linear markings pronounced well toward parenchyma; most marked on first day; persisted throughout series	Average size; smaller after 2nd day	Narrower upper mediastinal shadow on 2nd day than on 1st or 3rd; 2nd day film taken during expiration; others at end of inspiration
Rhi.	4,670	Linear markings pronounced throughout series; most pronounced on first day; incomplete aeration right upper lobe on 1st day	Average size; gradual decrease to 8th day; thereafter no change	Narrower upper mediastinal shadow after 2nd day
Sob.	2,860	Linear markings less pronounced than in other cases; no other changes made out	Much smaller shadow than any of series; unchanged during series	No change
Sac.	3,600	Linear markings pronounced well toward parenchyma; quite uniform intensity throughout	Average size; decided right-sided preponderance 1st day, smaller 3d day; unchanged thereafter	Upper mediastinal shadow about twice as large on 1st day as on 3rd day and thereafter uniformly as on 3rd day
Ren.	3,876	Linear markings pronounced well toward parenchyma; little or no change in density throughout series	Average size; definitely smaller after 2nd day	Upper mediastinal shadow definitely smaller on 7th day than on other days of series
Sap.	3,234	Linear markings pronounced well toward parenchyma; most pronounced on 2nd day; decidedly less marked on 3rd day and thereafter	Average size; definitely smaller after 2nd day	Upper mediastinal shadow gradually narrower after 1st day
Sca.	3,840	Linear markings pronounced; most pronounced on 2nd and 3rd days; seeming enlargement of hilum lymph nodes on 3rd day	Average size no noteworthy change	Upper mediastinal shadow definitely narrower after 2nd day; later films taken at full inspiration
Rit.	2,780	Linear markings pronounced—even more than average; most pronounced on 2nd day; thereafter diminished and quite uniformly so	Average size no noteworthy change	No noteworthy change
Sch.	3,550	Linear markings pronounced well toward parenchyma; most pronounced on 6th day; more pronounced on 1st and 2nd days than later except 6th day	Average size; definite right-sided preponderance 1st day; thereafter smaller and usual contour	No noteworthy change
Gri.	4,130	Linear markings pronounced throughout and quite uniformly so; caplike shadow right apex "like supposed atalect," 1st day; absent thereafter	Average size; smaller after 2nd day	Upper mediastinal shadow smaller after 1st day; 1st day film taken in expiration

TABLE 1.—*Roentgenographic Observations in Two Groups of Infants—Continued*

Name	Birth Weight Gm.	Pulmonary Fields	Cardiac Shadow	Mediastinum
Pul.	3,280	Linear markings quite pronounced; most pronounced 1st day; thereafter uniformly less	Average size; no noteworthy change	No noteworthy change
Fat.	3,560	Linear markings pronounced; most pronounced on 1st and 2nd days; thereafter uniformly less	Average size; larger on 2nd day with definite right sided prepond; thereafter usual contour	Definite gradual decrease in width of upper mediastinal shadow in 1st 4 days; thereafter quite uniform
Cla.	3,140	Linear markings pronounced; most pronounced on 1st and 2nd days	Average size; no noteworthy change	Definite change in mediastinal shadow (upper) with position of diaphragm
Fig.	3,120	Linear markings pronounced; definite hilum markings to 7th day; thereafter less pronounced; definite interlobar thickening; between right middle upper lobes 2nd day and throughout	Average size; no noteworthy change	Broad upper mediastinal shadow on 1st, 2nd and 3rd days—narrow 4, 5, 6, 7, 8, 9, 10; broad again 11, 12 (diaphragm position) narrow 13-14
Max.	4,670	Linear markings pronounced in 12 of 14 cases; most pronounced 1st day and 2nd day; atalectasis possible in case Grig; interlobar thickening Fig. and Rhi.	Smaller after 2nd day in 6 cases; very small heart-sob	Change in width of upper mediastinal shadow with respiration pronounced in Fig. and Cla.; narrower mediastinum after 2nd day in 6 cases
Min.	2,700			
Avg.	3,300			
		Second Group, Jan., 1926-May, 1926		
Zaf.	3,160	Linear markings pronounced well toward parenchyma; most marked in upper lobes on 12, 13, 14 days; definite interlobar thickening right lung, upper and middle lobes	Average size; smaller after 2nd day; thereafter uniform	Definite variation in width of upper mediastinum with diaphragm movements
Ser.	3,320	Linear markings pronounced throughout; uniformly so; definite interlobar shadow between right upper and middle lobes	Huge heart 1st day almost obliterating lung field; smaller 2nd day; average size thereafter	Definite variation in width of upper mediastinum with movements of diaphragm
Rea.	4,020	Linear markings pronounced throughout series; definite interlobar shadow between right upper and middle lobes	Average size; decrease after 6½ hours; definitely smaller after 2nd day	Definite variation in width of upper mediastinum with movements of diaphragm
Noe.	2,680	Linear markings pronounced throughout series; definite interlobar shadow (first seen 2nd day) between right upper and middle; thereafter persisted unchanged; peculiar shadow; lymph node found in left upper lobe	Average size; smaller after 1st day	No noteworthy change

TABLE 1.—*Roentgenographic Observations in Two Groups of Infants—Continued*

Name	Birth Weight Gm.	Pulmonary Fields	Cardiac Shadow	Mediastinum
Kau.	3,280	Linear markings pronounced; most marked on 1st and 2nd days; thereafter uniformly less; definite interlobar line on 4th day and thereafter	Average size; no noteworthy change	No noteworthy change
Lom. No. 1	3,340	Linear markings pronounced; uniformly so; definite interlobar line between right upper and middle lobes	Average size; definite decrease after 3rd day	No noteworthy change
Cip.	2,880	Linear markings less pronounced than average; fine peribronchial mottling found throughout series	Average size; no noteworthy change	No noteworthy change
Lom. No. 2	4,000	Linear markings pronounced for 1st and 2nd days, then much less marked; definite interlobar line between right upper and middle lobes	Average size; decrease in size after 2nd day	Persistently wide upper mediastinal shadow throughout series regardless of position of diaphragm
Bri.	3,280	Linear markings pronounced throughout series; most pronounced 1st and 2nd days; definite interlobar shadow only 1st day; bronchial plug, right upper lobe	Average size; no noteworthy change	No noteworthy change
Ale.	3,080	Linear markings present throughout series in average density; definite interlobar shadow on days 3, 4, 7, 10, 11 between right upper and middle lobes	Average size; no noteworthy change	No noteworthy change
Nel		Linear markings present throughout series, more dense than usual, especially on days 1, 2, 3; on 6th day peculiar circular density left lower lobe; absent on all other films; suggestion of interlobar thickening	Average size; decrease in size after 2nd day	Definite variation in width of upper mediastinal shadow with variation in position of diaphragm
Max. Min. Avg.	4,020 2,680 3,304	Linear markings pronounced in all cases; definite interlobar thickening in 9 of 10 cases; where intensity of linear markings varied, most intense on 1st and 2nd days; 3 instances of this observation: Kau., Lom. 2., Bri.	In 5 cases there was reduction in size after 2nd day; one case had huge heart (Ser.)	Definite variation in width of upper mediastinal shadow with the movements of the diaphragm in 3 instances, Zaf., Ser., Rea.; in one case persistently wide upper mediastinal shadow throughout regardless of movements of diaphragm (Lom. 2.)

COMMENT

Although it is clear from this brief study that sharp definition between daily roentgenograms of the first two weeks was not found, a certain progression and the regular occurrence of a number of interesting shadows deserve attention.

Among these shadows were the linear markings which extended so far toward the parenchyma of the lung. These were usually less distinct after the first three days, but they were at all times sufficiently dense to be taken for pulmonary disturbance. This misinterpretation might be avoided if the observer had a control series.

In the light of the recent work of Johnson and Meyers [4] who found evidence of pneumonia in ninety-seven (19 per cent) of 500 consecutive autopsies performed on stillborn and new-born babies, consideration must be given the possibility that these striking linear shadows could indicate a lesser degree of the same pulmonary disturbance. However, these babies appeared to be perfectly normal. They nursed well and gained well, and signs of disturbance were not elicited at any examination. Therefore, we have no choice but to believe these shadows to be normal (as far as can be determined by this series).

In common with previous observers, we found that accurate measurement of the size of the cardiac shadow was technically impossible. Likewise, the great individual variations in size and in cardiac contour made classification and description useless. The striking facts observed were the fairly regular tendency toward reduction in the size of the cardiac shadow after the second day, and the finding of a huge heart shadow in an apparently normal infant. It may be remembered that this shadow occupied almost the entire thoracic cavity during the first two days of life, yet cyanosis and other untoward symptoms were not observed, and cardiac murmurs were not heard. The subsequent films showed a cardiac shadow of proportions similar to those of other infants of this age.

Of considerable importance to the clinician were the films which illustrated Gerstenberger's observation that the width of the upper mediastinal shadow often changes most markedly with respiration, and in certain instances changes to the extent that it might readily be confused with the shadow interpreted as due to an enlarged thymus gland. This is particularly true if but a single film is seen and if that film is taken during expiration.

Our studies are in perfect agreement with Gerstenberger's statement that "it would seem as if the therapeutic roentgen-ray tests based on

4. Johnson, W. C., and Meyer, J. R.: A Study of Pneumonia in the Stillborn and New-Born, Am. J. Obst. & Gynec. **9**:151 and 167 (Feb.) 1925.

finding a normal shadow would be valueless unless checked by observations made at two different respiratory phases and especially with the aid of the fluoroscope."

A sort of composite of these consecutive roentgenograms of the thorax during the first fourteen days of life may be of some use: The roentgenograms made during the first twenty-four hours usually showed more dense linear pulmonary markings which extended further toward the parenchyma than on the second and subsequent days of this period. The interlobar pleural line between the right upper and middle lobes was almost regularly seen on the first day and varied little in density thereafter. The cardiac shadow was relatively larger on the first and second days.

In general, we feel that clinicians who deal with new-born babies will benefit by early recourse to the roentgenogram of the thorax in the study of obscure cases. Any decision concerning pneumonia can be made better if the interpreter has seen a complete daily series of roentgenograms of normal new-born babies.

95 Joralemon Street.

METABOLISM OF UNDERNOURISHED CHILDREN

IV. CALCIUM METABOLISM *

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CHICAGO

In the earlier papers of this series, the gain in weight while under care in the hospital,[1] the basal metabolism,[2] and the output of certain urinary constituents [3] of a group of undernourished children compared with that of a group of vigorous normal children were discussed. In the present paper, data concerning the calcium metabolism of ten normal and fifty undernourished children will be presented.

While the literature abounds with studies of the calcium metabolism of infants and its relation to the phosphorus and vitamin contents of the diet, little work has been reported on the calcium metabolism of undernourished children. In their study of calcium and phosphorus metabolism in childhood, Sherman and Hawley [4] summarized their own and the results of other investigators in a table which shows the average calcium retention of normal children to be 0.055 Gm. of calcium oxide per kilogram at the age of from 7 to 12 months, 0.015 Gm. at from 3 to 8 years, and 0.013 Gm. at from 9 to 14 years. (For convenience in comparison with our own results, we have recomputed Sherman's figures in terms of calcium oxide.) As a result of their own investigation, they report a calcium storage of from 0.010 to 0.020 Gm. of calcium oxide per kilogram a day, most of the children showing a storage of approximately 0.014 Gm. regardless of age, the range being from 0.024 to 0.081 Gm. on a diet containing 750 Gm. of milk.

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1. Wang, C. C.; Hays, B. B.; Frank, M., and Kern, R.: Metabolism of Undernourished Children: I. Gain in Weight, Am. J. Dis. Child. **32**:63 (July) 1926.

2. Wang, C. C.; Kern, R.; Frank, M., and Hays, B. B.: Metabolism of Undernourished Children: II. Basal Metabolism, Am. J. Dis. Child. **32**:350 (Sept.) 1926.

3. Wang, C. C.; Frank, M.; Kern, R., and Hays, B. B.: Metabolism of Undernourished Children: III. Urinary Nitrogen with Special Reference to Creatinine, Am. J. Dis. Child. **32**:360 (Sept.) 1926.

4. Sherman, H. C., and Hawley, E.: Calcium and Phosphorus Metabolism in Childhood, J. Biol. Chem. **53**:375 (Aug.) 1922.

TABLE 1.—*Calcium Metabolism of Vigorous Normal Children*

Subject	Age	Sex*	Weight		Calcium Oxide Intake		Calcium Oxide Output Per 24 Hours				Absorption			Retention		
			Kilograms	Per Cent Variation from Normal	Per 24 Hours (Gm.)	Per Kilogram Per 24 Hours (Gm.)	Urine (Gm.)	Feces (Gm.)	Total (Gm.)	Total Per Kilogram (Gm.)	Total (Gm.)	Per Kilogram (Gm.)	Per Cent of Intake	Total (Gm.)	Per Kilogram (Gm.)	Per Cent of Intake
M. S.	9	♂	33.5	+17.1	2.381	0.071	0.129	1.733	1.862	0.055	0.648	0.019	27.2	0.519	0.016	21.8
M. F.	8	♂	27.7	+ 8.6	1.390	0.050	0.186	0.952	1.138	0.041	0.438	0.016	31.5	0.252	0.009	18.2
M. H.	9	♂	23.9	+ 3.2	1.457	0.061	0.230	0.844	1.074	0.045	0.613	0.026	42.1	0.383	0.016	26.3
S. A.	10	♀	29.2	+ 1.4	1.658	0.057	0.042	1.348	1.390	0.048	0.310	0.011	18.7	0.268	0.009	6.2
L. L.	10	♂	34.0	+ 1.2	2.431	0.072	0.128	2.010	2.138	0.063	0.421	0.012	17.3	0.293	0.009	16.2
B. L.	12	♂	33.0	+ 1.2	2.721	0.082	0.173	2.261	2.434	0.073	0.460	0.014	16.9	0.287	0.009	10.5
A. G.	5	♀	17.9	+ 0.6	2.063	0.114	0.290	1.593	1.883	0.105	0.440	0.025	21.6	0.150	0.008	7.4
F. J.	11	♀	28.2	+ 0.6	2.068	0.073	0.044	1.545	1.589	0.057	0.523	0.019	25.3	0.480	0.017	23.2
S. W.	8	♀	21.9	— 1.4	2.473	0.113	0.376	1.846	2.222	0.102	0.627	0.028	25.4	0.251	0.011	10.1
H. S.	9	♀	27.2	— 3.5	1.515	0.057	0.061	1.132	1.193	0.045	0.383	0.014	25.3	0.322	0.012	21.3
Average	9.1	..	....	+ 2.9	.....	0.075	.....	.....	.....	0.063	.....	0.018	25.1	.....	0.012	16.1

* In this table and in tables 2, 3, 4 and 5, ♂ indicates male and ♀, female.

TABLE 2.—*Calcium Metabolism of Children Normal in Weight Only*

Subject	Age	Sex	Weight		Calcium Oxide Intake		Calcium Oxide Output Per 24 Hours				Absorption			Retention		
			Kilograms	Per Cent Variation from Normal	Per 24 Hours (Gm.)	Per Kilogram Per 24 Hours (Gm.)	Urine (Gm.)	Feces (Gm.)	Total (Gm.)	Total Per Kilogram (Gm.)	Total (Gm.)	Per Kilogram (Gm.)	Per Cent of Intake	Total (Gm.)	Per Kilogram (Gm.)	Per Cent of Intake
E. F.	6	♀	19.3	+ 4.9	1.215	0.063	0.063	0.937	1.000	0.052	0.278	0.014	22.8	0.215	0.011	17.7
R. M.	5	♂	14.4	± 0.0	1.339	0.093	0.089	1.137	1.226	0.085	0.202	0.014	15.1	0.113	0.008	8.4
H. D.	5	♂	13.8	± 0.0	1.301	0.094	0.098	0.931	1.029	0.075	0.370	0.027	28.4	0.272	0.019	20.9
J. G.	8	♂	23.8	— 0.0	2.534	0.106	0.141	1.903	2.044	0.085	0.631	0.027	24.9	0.490	0.021	19.3
E. G.	6	♂	18.1	— 1.1	1.279	0.071	0.092	1.005	1.097	0.061	0.274	0.015	21.4	0.182	0.010	14.2
N. G.	7	♂	16.9	— 1.2	1.249	0.074	0.096	0.868	0.964	0.057	0.381	0.023	30.5	0.285	0.017	22.8
E. G.	6	♀	17.5	— 1.7	1.375	0.079	0.119	0.805	0.924	0.053	0.570	0.033	41.5	0.451	0.026	32.8
G. L.	13	♀	34.7	— 3.3	1.460	0.042	0.174	1.180	1.354	0.039	0.280	0.008	19.2	0.106	0.003	7.3
N. G.	7	♂	16.5	— 3.5	1.211	0.073	0.151	1.013	1.164	0.071	0.198	0.012	16.3	0.047	0.003	3.9
K. B.	8	♀	20.7	— 3.7	1.747	0.084	0.105	1.281	1.386	0.067	0.466	0.022	26.6	0.361	0.017	20.6
E. G.	6	♀	17.5	— 3.8	1.329	0.076	0.108	1.095	1.203	0.069	0.234	0.013	17.6	0.126	0.007	9.4
I. B.	10	♂	30.5	— 4.1	1.739	0.057	0.207	1.392	1.599	0.053	0.338	0.011	19.5	0.131	0.004	7.6
E. F.	6	♀	17.3	— 4.9	1.216	0.070	0.053	0.816	0.869	0.047	0.400	0.023	32.9	0.347	0.020	28.5
Average	7.2	..	....	— 1.7	.....	0.076	.....	.....	.....	0.063	.....	0.019	24.1	.....	0.013	16.4

TABLE 3.—*Calcium Metabolism of Children from 5.1 to 10 Per Cent Underweight*

Subject	Age	Sex	Weight		Calcium Oxide Intake		Calcium Oxide Output Per 24 Hours				Absorption			Retention		
			Kilograms	Per Cent Variation from Normal	Per 24 Hours (Gm.)	Per Kilogram Per 24 Hours (Gm.)	Urine (Gm.)	Feces (Gm.)	Total (Gm.)	Total Per Kilogram (Gm.)	Total (Gm.)	Per Kilogram (Gm.)	Per Cent of Intake	Total (Gm.)	Per Kilogram (Gm.)	Per Cent of Intake
W. K.	12	♂	28.6	— 5.3	1.788	0.063	0.257	1.192	1.449	0.051	0.596	0.021	33.3	0.339	0.012	18.9
G. C.	10	♂	26.9	— 5.3	1.813	0.067	0.157	1.411	1.568	0.058	0.402	0.015	22.2	0.245	0.009	13.5
E. B.	5	♀	15.8	— 5.4	1.350	0.085	0.083	1.005	1.088	0.069	0.345	0.022	39.0	0.262	0.017	19.0
J. G.	8	♂	22.4	— 5.9	1.446	0.065	0.106	1.144	1.250	0.056	0.302	0.014	20.9	0.196	0.009	13.6
A. Go.	10	♀	27.6	— 6.1	1.941	0.070	0.157	1.578	1.735	0.063	0.363	0.013	18.7	0.206	0.008	10.6
R. G.	6	♂	16.3	— 7.9	1.335	0.082	0.079	1.129	1.208	0.074	0.206	0.014	15.4	0.127	0.008	9.5
L. C.	6	♀	18.7	— 7.9	1.339	0.072	0.087	0.859	0.946	0.051	0.480	0.026	35.9	0.393	0.021	28.6
E. D.	10	♂	25.0	— 8.1	1.538	0.062	0.041	1.166	1.207	0.048	0.372	0.015	24.2	0.331	0.013	21.5
J. U.	9	♀	25.9	— 8.2	1.810	0.070	0.148	1.349	1.497	0.058	0.461	0.018	25.5	0.313	0.012	17.3
E. G.	6	♀	16.3	— 8.4	1.100	0.067	0.072	0.736	0.808	0.050	0.364	0.022	33.1	0.292	0.018	26.5
B. G.	9	♀	20.5	— 8.5	1.588	0.077	0.094	1.126	1.320	0.064	0.462	0.023	29.1	0.268	0.013	16.9
H. K.	10	♂	21.7	— 8.8	1.480	0.068	0.098	0.955	1.053	0.049	0.525	0.024	35.5	0.462	0.021	28.8
L. C.	6	♀	18.4	— 9.4	1.411	0.077	0.043	1.018	1.061	0.058	0.393	0.021	27.9	0.350	0.019	24.8
C. S.	10	♂	27.0	— 9.4	1.823	0.068	0.104	1.317	1.421	0.053	0.506	0.019	27.8	0.402	0.015	22.1
S. K.	10	♂	27.5	— 9.8	2.253	0.082	0.112	1.743	1.855	0.068	0.510	0.018	22.6	0.398	0.014	17.7
T. F.	10	♂	23.4	— 9.8	1.762	0.075	0.100	1.121	1.221	0.052	0.641	0.027	36.3	0.541	0.023	30.7
Average	8.5	..	....	— 7.8	.....	0.072	.....	.....	.....	0.058	.....	0.020	28.0	.....	0.015	20.0

TABLE 4.—*Calcium Metabolism of Children from 10.1 to 15 Per Cent Underweight*

Subject	Age	Sex	Weight		Calcium Oxide Intake		Calcium Oxide Output Per 24 Hours				Absorption			Retention		
			Kilograms	Per Cent Variation from Normal	Per 24 Hours (Gm.)	Per Kilogram Per 24 Hours (Gm.)	Urine (Gm.)	Feces (Gm.)	Total (Gm.)	Total Per Kilogram (Gm.)	Total (Gm.)	Per Kilogram (Gm.)	Per Cent of Intake	Total (Gm.)	Per Kilogram (Gm.)	Per Cent of Intake
M. S.	9	♀	21.6	—10.4	1.479	0.068	0.101	0.929	1.030	0.048	0.520	0.024	35.1	0.449	0.021	30.4
K. Bo	8	♀	20.6	—10.5	1.770	0.086	0.041	1.277	1.318	0.064	0.493	0.024	27.9	0.452	0.022	25.5
H. L.	8	♀	19.3	—10.6	1.585	0.082	0.088	1.110	1.198	0.062	0.475	0.025	30.0	0.387	0.020	24.4
H. G.	11	♂	27.5	—10.7	1.945	0.071	0.112	1.415	1.527	0.056	0.530	0.019	27.3	0.418	0.015	21.5
E. S.	4	♀	13.7	—11.0	0.932	0.068	0.024	0.561	0.585	0.043	0.371	0.027	39.8	0.347	0.025	37.3
L. C.	6	♀	18.0	—11.3	1.375	0.076	0.116	0.806	0.922	0.051	0.569	0.032	41.4	0.453	0.025	32.9
M. M.	7	♂	17.9	—11.8	1.313	0.073	0.105	0.951	1.056	0.059	0.362	0.020	27.6	0.257	0.014	19.6
B. B.	5	♀	12.0	—11.8	1.237	0.103	0.041	0.856	0.897	0.075	0.381	0.032	30.8	0.340	0.028	27.5
S. K.	10	♂	26.8	—12.1	2.399	0.090	0.109	1.893	2.002	0.075	0.506	0.019	21.1	0.397	0.015	16.5
J. M.	13	♂	27.5	—12.1	2.465	0.090	0.176	2.031	2.207	0.080	0.434	0.016	17.6	0.258	0.009	10.5
R. D.	10	♀	19.1	—12.3	1.766	0.093	0.087	1.369	1.456	0.076	0.397	0.021	22.3	0.310	0.016	17.4
N. G.	7	♂	15.0	—12.3	1.532	0.102	0.070	1.145	1.215	0.081	0.387	0.026	25.2	0.317	0.021	20.7
F. B.	10	♀	17.8	—13.2	1.686	0.095	0.093	1.211	1.304	0.073	0.475	0.027	28.2	0.382	0.021	22.7
E. F.	6	♀	15.4	—13.5	1.221	0.079	0.046	0.958	1.004	0.065	0.263	0.017	21.4	0.217	0.014	17.8
B. G.	8	♀	19.1	—13.6	1.440	0.075	0.093	1.109	1.202	0.063	0.331	0.017	23.0	0.238	0.012	16.5
R. B.	6	♂	16.4	—14.1	1.402	0.085	0.045	1.084	1.129	0.069	0.318	0.019	22.7	0.273	0.017	19.5
Average	8	..	....	—12.0	.....	0.084	.....	.....	.....	0.065	.....	0.023	27.6	.....	0.018	22.5

In their study of the difference in calcium retention on diets containing pasteurized as compared with evaporated milk, Willard and Blunt [5] found an average retention of from 0.010 to 0.039 Gm. (as calcium oxide) per kilogram for four children ranging in age from 3 to 12 years and having a total calcium intake of from 1.41 to 1.86 Gm. of calcium oxide a day. These diets contained from 810 to 825 Gm. of milk.

EXPERIMENTAL

Sixty children, nineteen boys and forty-one girls, ranging from 4 to 13 years in age, were used as subjects in this experiment. As already stated, ten of them were vigorous normal children and fifty were underweight, including nine whose weight was not more than 5 per cent below the Baldwin-Wood standard, but who nevertheless showed the physical signs of malnutrition. The arbitrary division used in previous studies,[3] which placed the children into five groups according to the degree of underweight, was also used in this study. A number of the children were kept at the hospital for comparatively long periods, and studies were made on them from time to time in order to observe any metabolic change which might be taking place during a period of gain in weight. Therefore, a number of the same children appear in the table more than once.

The children lived in the hospital for from ten days to twenty-three weeks, subject to the physical care described in the first paper of this series.[1] The subjects were placed on a weighed diet for at least six days. A twenty-four hour specimen of urine and a three day specimen of feces were collected during the last three days of the period. The same technic in the collection of specimens and in the analysis of foods and excreta was observed as has already been reported in our previous papers.[6]

COMMENT

Fifty-seven per cent of all the children in the five groups had an intake of between 0.06 and 0.08 Gm. of calcium oxide per kilogram a day. Thirty-four per cent had an intake of more than 0.08 Gm., and only 9 per cent less than 0.06 Gm. The minimum intake of 0.042 Gm. occurred in only one case. On the whole our subjects show a considerably higher intake than those of Sherman, as only four of the twelve children that he studied had an intake of 0.06 Gm. or more, while most of them ate much less than this. A marked difference is not found in the intake of the different groups in our experiment, although the fourth group shows a slightly higher average, due to the larger number of children in this group who ate more than 0.08 Gm. per kilogram.

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5. Willard, A. C., and Blunt, K.: A Comparison of Evaporated with Pasteurized Milk as a Source of Calcium, Phosphorus and Nitrogen, J. Biol. Chem. **75**:251 (Oct.) 1927.

6. Footnote 3. Wang, C. C.; Witt, D. B., and Felsher, A. R.: A Comparison of the Metabolism of Some Mineral Constituents of Cow's Milk and of Breast Milk in the Same Infant, Am. J. Dis. Child. **27**:352 (April) 1924.

TABLE 5.—*Calcium Metabolism of Children More Than 15 Per Cent Underweight*

Subject	Age	Sex	Weight		Calcium Oxide Intake		Calcium Oxide Output Per 24 Hours				Absorption			Retention		
						Per Kilogram										
			Kilograms	Per Cent Variation from Normal	Per 24 Hours (Gm.)	Per 24 Hours (Gm.)	Urine (Gm.)	Feces (Gm.)	Total (Gm.)	Total Per Kilogram (Gm.)	Total (Gm.)	Per Kilogram (Gm.)	Per Cent of Intake	Total (Gm.)	Per Kilogram (Gm.)	Per Cent of Intake
L. C.	6	♀	17.1	—15.8	1.247	0.073	0.137	0.811	0.948	0.055	0.436	0.025	35.0	0.299	0.017	24.0
D. Y.	7	♀	17.3	—16.0	1.290	0.075	0.036	1.180	1.216	0.070	0.110	0.006	8.5	0.074	0.004	5.7
E. F.	6	♀	15.2	—16.5	1.194	0.079	0.050	0.940	0.991	0.065	0.254	0.017	21.2	0.203	0.013	17.0
S. K.	10	♂	25.4	—16.7	2.280	0.090	0.072	1.790	1.862	0.073	0.490	0.019	21.5	0.418	0.016	18.3
A. S.	10	♀	17.8	—16.8	1.230	0.069	0.015	1.065	1.080	0.061	0.165	0.009	13.4	0.150	0.008	12.2
L. B.	11	♀	25.8	—17.8	2.432	0.094	0.099	1.905	2.004	0.078	0.527	0.020	21.6	0.427	0.017	17.6
A. B.	6	♀	16.9	—18.0	1.220	0.072	0.052	0.790	0.840	0.050	0.430	0.025	35.2	0.380	0.022	31.1
A. S.	10	♀	17.4	—18.7	1.459	0.084	0.050	1.073	1.123	0.065	0.386	0.022	25.8	0.336	0.019	23.0
A. S.	10	♀	16.9	—19.2	1.555	0.092	0.014	1.254	1.268	0.075	0.301	0.018	19.4	0.287	0.017	18.5
L. P.	8	♀	22.6	—19.8	1.531	0.068	0.074	1.026	1.100	0.049	0.505	0.022	33.0	0.431	0.019	28.2
A. Go	10	♀	20.6	—23.4	1.770	0.086	0.108	1.400	1.508	0.073	0.370	0.018	20.9	0.262	0.013	14.8
R. N.	11	♀	25.2	—25.0	1.420	0.056	0.122	1.082	1.204	0.048	0.338	0.013	23.8	0.216	0.009	15.2
A. G.	8	♀	17.9	—25.7	1.338	0.075	0.122	0.872	0.994	0.056	0.466	0.026	34.8	0.344	0.019	25.7
Average	8.7	..	....	—19.2	.....	0.078	.....	.....	.....	0.063	.....	0.019	24.2	.....	0.015	19.3

The average excretion is practically the same in all groups. Three of five had an average of 0.063 Gm. of calcium oxide per kilogram. The other two show averages of 0.069 and 0.058 Gm. The maximum individual excretion was 0.105 Gm. and the minimum, 0.041. Both of these extremes occurred in the vigorous normal group.

The calcium absorption shows wide individual variations in all five groups, ranging from 0.009 to 0.033 Gm. of calcium oxide per kilogram, and from 13.4 to 42.1 per cent of the calcium intake. The averages, however, of the five groups seem to show a slight increase in absorption in groups 3 and 4. The averages of the other three groups, the vigorous normal children, those normal in weight only, and those 15 per cent or more underweight, are practically the same.

In the same manner, the calcium retention also varies widely in all groups, ranging from 0.003 to 0.028 Gm. of calcium oxide per kilogram. Again, in groups 3 and 4 a slight increase is noted in the average retention, although in every group the average retention is higher than that observed by Sherman.

From the foregoing figures, it would appear that the capacity of undernourished children for the absorption and retention of calcium is in every way normal. Attention should again be called to the fact that the calcium intake of our subjects was higher than the standard set by Sherman. In spite of this fact, it is interesting to note that the undernourished children were not storing calcium at a much more rapid rate than the vigorous normal children. The trend seems to be in the direction of a slight increase in calcium storage in the underweight groups, due to the fact that the children probably had been on diets too low in calcium before they entered the hospital. The apparent slight increase in the average retention per kilogram of weight in groups 3 and 4 is probably due to this fact and also to the fact that the loss in weight in these groups is due to a reduced amount of fatty tissue, and therefore, estimated per kilogram of body weight, the retention appears to be higher.

Evidently, as has been previously stated, the underweight child is not underweight because of any abnormalities in metabolism, but because of an insufficient and unsatisfactory diet.

SUMMARY

The results of an investigation of the calcium metabolism of ten normal and fifty undernourished children are reported in this paper.

The calcium absorption and retention showed wide individual variations among both normal and undernourished children.

A slight tendency toward increased calcium storage was noted among the underweight children.

Case Reports

PSEUDOHERMAPHRODISM (FEMALE TYPE PREDOMINATING) *

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AND

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It is not our purpose to attempt to cover the subject of hermaphrodism or even the various types of internal, external, complete or secondary pseudohermaphrodism. To those interested in this phase of the subject may be referred some of the literature encountered by us; namely, articles by Bell,[1] Goldjanitzki,[2] Kreuter,[3] Quimby,[4] Thorek,[5] Gibson[6] and others. We considered this case, however, to be one of sufficient rarity and interest to be included in the literature, and, furthermore, the satisfactory result prompted us to report it. The child was fortunately brought to our attention early enough to spare her the humiliation of being conscious of being different from her associates. As Bell[1] states, the secondary sex characteristic in all cases of partial hermaphrodism are opposite in type to the declared sex of the gonads. However, in spite of this, it was deemed essential to determine the primary sex of the child before amputation of the phallus, and it was for this reason that she was subjected to an external examination under ether and an exploratory abdominal operation at a later date.

* Received for publication, Jan. 25, 1928.

* From the Department of Pediatrics, the Cottage Hospital Dispensary.

1. Bell, W. Blair: Hermaphroditismus Externus Femininus, Am. J. Obst. & Gynec. **10**:778 (Dec.) 1925.

2. Goljanitzki, J. A.: Surgical Treatment of Hermaphrodites, Arch. f. klin. Chir. **144**:732, 1927.

3. Kreuter, E.: Transplantation of the Testicle, Zentralbl. f. Chir. **49**:538 (April) 1922.

4. Quimby, W. C.: Pseudo Hermaphrodism, Bull. Johns Hopkins Hosp. **27**:50 (Feb.) 1916.

5. Thorek, M.: Some Clinical Aspects of Human Sex Gland Maldevelopment and Its Possible Relief, M. J. & Rec. **123**:743 (June 2) 1926.

6. Gibson, T. E.: The Diagnosis of Adrenal Tumors, J. Urol. **18**:33, 1927.

CASE REPORT

History.—A. B., aged 11½ years, was referred to the children's service of the outpatient department of the Cottage Hospital on June 10, 1927, by Dr. E. J. Lamb, the medical inspector of the Santa Barbara public schools. The physician who delivered the child first noticed the condition and told the mother it would be outgrown. The voice had always been heavy and coarse. Progress in school had been exceptionally good, and the child got on well with other children. The mother thought the patient did not have any idea of her condition. Pubic hairs appeared

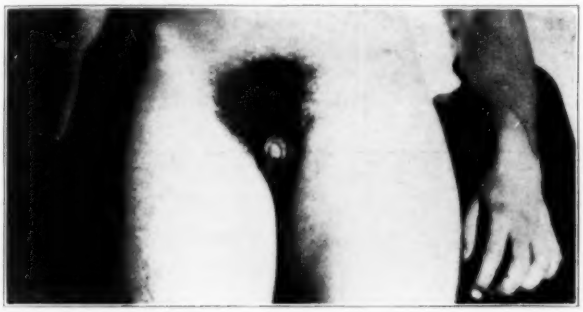

Fig. 1.—Photograph showing the male type of pubic hair.

Fig. 2.—Showing the size of the phallus.

when she was about 10½. The mammary glands had become enlarged during the last two or three months before she came to the hospital. Menstruation had not occurred. The school nurse's attention was first attracted to the child by her deep voice. Birth had been normal, the child weighing 5 pounds (2 Kg.). She had been breast fed only a few weeks. The child sat up at 1 year of age and talked at 2 years. The teeth had developed at the normal time. She had walked when she was 1½ years old. Except for an attack of influenza and whooping cough, she had always been well. The mother and father were both well. One brother, 14 years of age, was well. There were three sisters married and well. Three children had died; one, a "blue baby," died a few hours after birth; one died of influenza and one died of mastoiditis.

Physical Examination.—The physical development was good, although the child was overweight and overheight for her age.

There was a moderate hypertrichosis on the upper lip, chin, both arms and thighs. The complexion was dark. The teeth were good. The nose and ears were normal.

An examination of the eyes did not reveal any strabismus or nystagmus. The reaction to light was sluggish, and the pupils were equal. The tonsils were small and embedded, but not septic. The pharynx was slightly red.

The superficial glands were normal.

Formation of the chest was good, and the lungs were normal.

The heart was not enlarged; the sounds were clear; the rate and the rhythm were normal.

The abdomen was soft, and there were not any masses or tenderness that could be made out. The liver and the spleen were not palpable.

Fig. 3.—Showing hypospadias and external genitalia.

The extremities were normal. The knee jerks were equal and accentuated.

Examination was not made of the genitals. The vagina appeared normal. The clitoris was extremely large, and had the appearance of a rudimentary penis about 1½ inches (4 cm.) in length and ¾ inch (2 cm.) in diameter.

Pelvic Examination.—On Aug. 15, 1927, the child was admitted to the Cottage Hospital, where a pelvic examination was made under ether anesthesia, by Dr. Samuel Robinson. There was an abundance of crotch hair similar to that of the male; the pubic hair was triangular, with a small line up to the umbilicus. A tiny, meatal, nonpatent opening was found on the tip of the glands. Below the phallus and extending downward was a well marked hypospadia. The vaginal opening admitted two fingers; a female type of urethra was present. The labia majora were well marked. On palpation, a cervix could be felt and seen by the aid of a speculum. Little could be felt in the region of the ovaries. Masses or other structures resembling ovaries could not be made out. The uterus felt rather poorly developed and seemed to fade away from the cervix. Testes were not felt in the region of the groin.

Rectal examination did not reveal any masses in the region of the prostate.

Exploratory Operation.—On Aug. 22, 1927, Dr. Robinson performed an exploratory operation to determine the exact primary sex of the child. The uterus was rudimentary, very much undeveloped, with apparently normal appearing tubes and ovaries. A small cyst was attached to one of the ovaries; this was removed. Masses were not felt in the region of the kidneys (pathologic masculinity in early life is often associated with suprarenal hyperplasia and neoplasia). Both flanks were opened and search made for the presence of testes or tissue resembling them. No such tissue was found. As fairly normal female internal organs were found, the sex of the child was definitely considered female. The sex being determined by the laparotomy and the plastic operation on the vulva, the phallus was amputated by Dr. Robinson. A good recovery was made.

A pathologic report of a section made by Dr. Nuzum and Dr. Evans from the small mass removed from the ovary, gave the diagnosis of a simple ovarian cyst.

The amputated phallus was 7 by 2 cm. and consisted essentially of two parts. The glands were normal in appearance and about 1.5 cm. long. A urethral opening was not seen; the body consisted of two corpori carvernosi. On section, there was no evidence of an urethra.

Histology.—In the four sections examined, there were muscular and fibrous tissues with large cavernous blood sinuses. Skin existed along one surface of two sections; evidence of an urethral opening was not apparent.

The diagnosis was erectile tissue with nothing distinctive as to sex present.

CONCLUSIONS

Without using any particular classification or nomenclature, we consider that we were dealing with a pseudohermaphrodism with the female type predominating.

JUVENILE TABES DORSALIS

REPORT OF THREE CASES *

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Because of the rare occurrence of tabes dorsalis in children, it seems worth while to report my observations in three cases. In more than 7,000 consecutive cases of nervous diseases in the Children's Hospital in Boston, not a single case of tabes appeared.[1] In Abt's "Pediatrics" it is stated that only sixty true instances are recorded in the literature as occurring before the fifteenth year. Perhaps one reason for this may be as Hutinel[2] says, "Doubtless it was confused with Friedreich's disease." That it is an extremely rare disease of childhood, however, is certain. Referring to juvenile tabes dorsalis and juvenile general paralysis, Sachs and Hausman[3] in their late textbook say, "These forms are so rare that Sachs did not mention them in his former textbook." They say further: "Personal experience has convinced us that they deserve brief notice if errors are to be avoided." In many textbooks, juvenile tabes is dismissed with a remark concerning its rarity and a statement that it is similar to adult tabes dorsalis. Observers who have evidently had an opportunity to study these cases early and follow them have noted important differences in juvenile tabes.

REPORT OF CASES

CASE 1.—*History.*—R. B., a colored boy, born Jan. 21, 1917, was brought to the syphilis clinic of the Children's Memorial Hospital on March 4, 1926; he was not able either to see or to stand alone. When 1 year of age, he had been treated for syphilis with a gray powder during a period of one month. At 6 years of age he began to run into objects so that the family decided that his vision must be affected. He was accordingly taken to the eye department of a dispensary where, in 1924, a diagnosis of optic atrophy due to syphilis was made. In December, 1925, he could walk alone, but at the time of my first contact with him in March, 1926, he was no longer able to stand alone.

Before the birth of the patient, there had been two spontaneous abortions at four and six months. When the patient was 1 year and 6 months of age, the mother had a stillbirth, and when he was 3 years of age, a younger brother was born. This brother was syphilitic and is now under treatment in this clinic. The syphilis was thus apparently rather virulent.

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* Received for publication, Feb. 7, 1928.

* From the Syphilis Clinic at the Children's Memorial Hospital.

1. Fairbanks, Arthur W, in Abt's Pediatrics, Philadelphia, W. B. Saunders Company, 1925, vol. 7, p. 606.

2. Hutinel, V.: Le terrain heredo syphilitique, Paris, Masson & Cie., 1926.

3. Sachs and Hausman: Nervous and Mental Disorders, New York, Paul B. Hoeber, 1926, p. 272.

There was a history of early snuffles, but the mother said that he had had them until the adenoids were removed when he was 4 years of age. There was no history of a rash nor of any other symptom suggestive of syphilis.

Physical Examination.—On March 4, 1926, examination revealed a fairly well nourished and a rather well developed colored boy, aged 9, measuring 47.5 inches (102.8 cm.) in height and weighing 50 pounds (22.7 Kg.). He was unable to stand even when the legs were placed in such a position that they made a broad base. When he was supported, attempts at walking resulted in the typical flaccid gait of tabes with the legs raised high, swung around and slapped down. Tests for muscle sense and coordination, such as placing the heel against the opposite knee and the finger against the tip of the nose, were not successfully performed.

Nystagmus of the ocular type was present and a divergent strabismus. The pupils were dilated; the right was larger than the left, and there was no reaction to either light or distance. The knee jerks were entirely absent, as were also the cremasteric and abdominal reflexes. Ankle clonus was absent. The epitrochlear nodes were the size of peas. The liver and spleen were not felt. Calluses, scars, ulcers or other skin lesions were not present, nor were there any bony lesions. The testicles were normal. The fundi examined by Dr. R. Gamble showed a marked atrophy of each disk.

The mentality was good, and there was no history or evidence of any sphincteric disturbance. Skin sensation to pain, heat, cold and touch seemed normal.

The Wassermann reactions of the blood and spinal fluid were four plus, and the Lange reaction on the spinal fluid was 2233210000.

At this stage, the patient had the symptoms typical of adult tabes in the paralytic stage, namely pupillary rigidity, optic atrophy, loss of reflexes, ataxia, paralysis and a positive spinal fluid reaction. The advanced stage of the disease and its continuous rapid advancement is different from the type usually encountered in childhood, exemplified by cases 2 and 3 in this report.

On later examinations in July and August, it was noticed that as the patient lay supine on the table, that he was flaccid but that on being raised to the upright position, an extensor spasm of the legs resulted which tended to take the scissors position so often seen in Little's disease. When the patient was supported and encouraged to walk, his attempts were characterized by high steps and walking on the outer border of the feet, especially the right, and the right foot sometimes caught behind the left, the muscles of the arms and trunk were not involved in this spasm. This was different from the previously noted attempts at walking, which were characteristic of tabes dorsalis.

From this change it was evident that syphilitic process had invaded the pyramidal tracts. The former picture of tabes dorsalis in the paralytic stage was changed to one of cerebrospinal syphilis with a pyramidal tract syndrome.

CASE 2.—*History.*—L. C., a white girl, born Sept. 2, 1920, was admitted to the hospital on June 22, 1926, because of pain in the abdomen, vomiting and a generally poor condition. The pain and vomiting had been present for about a month, occurring for one or two days followed by a free interval of a few days. The patient was emaciated, dehydrated and seemed acutely ill.

Physical Examination.—The pupils were equal, slightly irregular, dilated and reacted to neither light nor accommodation. There were no posterior or anterior synechiae present. The teeth were poor. Patellar and achilles reflexes were increased. Babinski, Brudzinski and Kernig signs were negative. Clonus was not present. The epitrochlear nodes were the size of peas. An examination

between attacks after the weakness of the attack had passed showed that there was no unsteadiness of gait and no ataxia of the arms or legs; Romberg's sign was absent. Attempts made to test cutaneous sensation seemed to show that there was no disturbance present. The fundi were normal.

Examination of the spinal fluid revealed: globulin present, 30 cells, sugar 64 mg. per hundred cubic centimeters. The Wassermann test was four plus. The Lange reaction was reported as 1233200000. The blood Wassermann reaction was also four plus.

The attack for which the patient was admitted on June 22, 1926, stopped abruptly during the following evening, and the child immediately took fluids well by mouth. On June 26, 1926, she had a short attack; she also had one on June 30. Another attack did not occur until July 14, when vomiting began abruptly after abdominal pain. This abdominal pain was of varying intensity and always preceded vomiting sometimes by a few minutes and again by as long as a few hours. The pain was in the upper part of the abdomen but was not definitely localized, and there was no tenderness. The occurrence of pain previous to the vomiting, as in this case, helps one to rule out the possibility that the attack is one of cyclic vomiting. Pain sometimes follows the vomiting in cases of cyclic vomiting as a result of violent vomiting, but it does not precede the vomiting as it invariably does in this type of patient.

An unusual accompaniment of the vomiting in this case was a rise in the blood pressure to about 140 systolic and 100 diastolic, whereas between attacks it was about 110 systolic and 80 diastolic.

These attacks of pain and vomiting have continued to recur, and they last from ten hours to as long as five days. Usually, however, the attacks remain two or three days. The interval between attacks varies from two days to as long as twenty-two days, but the attacks often recur at intervals of about ten days.

This has continued now more than a year, and during this time there has been no progression of symptoms. The patient has spent much of the time in the solarium of the hospital. For this reason and on account of antisyphilitic treatment, the general condition is now better than it was at the time of admission.

CASE 3.—*History.*—D. C., a white girl, born Oct. 18, 1917, was first seen by me in November, 1924, when she was brought to the dispensary of the Children's Memorial Hospital because of restlessness during the night and loss of weight. The mother had died at the time of the child's birth, and the latter had been fostered by the mother's sister. I was never able to learn any of the details concerning the mother, except that the foster mother told me that this was the only pregnancy. Nothing was known of the father.

Physical Examination.—Examination revealed a thin, pale girl with dry skin. She was a decided mouth breather. The tonsils were large, irregular and cryptic, and the teeth had considerable defect in the enamel. The spleen was definitely palpable. The right epitrochlear node was the size of a large pea; the left was that of a regular-sized pea. There was moderate anterior bowing of the tibiae. Knee jerks were present and equal, and the abdominal reflexes were brisk. Romberg's sign was absent. There was apparently no disturbance in cutaneous sensation. The Wassermann reactions of the blood and spinal fluid were four plus. Globulins were present, and the Lange colloidal gold test was reported 544432111.

The pupils were dilated and did not react to either light or accommodation. The right was a little larger than the left, and they were regular. A convergent squint was present. There was no ptosis or nystagmus.

On Feb. 14, 1925, the patient fell down stairs and fractured both bones of the right forearm at the lower third. The fracture gave almost no pain, and reduction, which had to be done twice because of a poor position the first time, was painless and was accomplished without an anesthetic. Healing followed normally.

On Aug. 13, 1925, the patient had severe shooting pains in the abdomen followed by a severe attack of vomiting. There was no tenderness or rigidity in the abdomen, and there was no fever during the attack. The attack came on abruptly and stopped abruptly after four days. Attacks similar to this one appeared from every three to every six months as long as I had the care of the patient, until June, 1926. Following an attack on May 13, 1925, she suffered from herpes zoster over the left buttocks extending anteriorly over the left side of the vulva.

The patient is now under the care of a private physician, who reports that her condition is much as it was. She has attacks of these gastric crises and vomiting every few months as when I was treating her.

COMMENT

The condition in case 1 (R. B.), unlike that in cases 2 and 3, is evidently rapidly progressive. On Christmas, 1925, the patient could walk but in the following March, the time of my first contact with him, he could no longer stand alone. The involvement of the pyramidal tracts in a few months is further evidence of the rapid course of the disease.

The condition in cases 2 and 3 is of the type more commonly seen in children. It corresponds closely to the description of Ibrahim [4] who, says in referring to juvenile tabes dorsalis: "Ataxia and gait disturbances are seldom seen and the pattelar reflex is not always lost." He says further: "The malady terminates beyond the years of childhood." Babinski [5] refers to these types of cases as "formes frustes," and he says that they do not call attention to themselves and ought to be studied carefully. The patients decline slowly, and Batten says: [6] "Complete incapacity may not occur until toward the end of the second decade of life." Thus the incomplete picture of tabes continued over a long period and the passing of many years before the loss of the deep tendon reflexes and the development of ataxia seem characteristic of juvenile tabes, and Babinski's phrase "formes frustes" seems well chosen.

The third case (D. C.) seems especially interesting because of the crises, the neuropathic fracture and the herpes zoster following an attack of gastric crisis. Referring to these fractures, Church [7] says

4. Feer: Lehrbuch der Kinderheilkunde, Jena, Gustav Fischer, 1921.

5. Babinski, quoted by Hutinel (footnote 2).

6. Garrod, Batten and Thursfield: Disease of Children, London, Arnold, 1913, p. 850.

7. Church, A.: Diseases of the Nervous System, New York, D. Appleton & Company, 1911, p. 491.

that they sometimes appear during the early stages, may follow insignificant trauma, run their course without pain, and heal well under appropriate treatment. Regarding the herpes zoster, it is said [8] that this skin disturbance is common in tabetic patients, and that it is due to the anatomic changes in the nerve roots and spinal ganglia.

In all three of these patients, the observations on the eye were significant. The vision in cases 2 and 3 was good, and the fundi were normal. In case 1, entire loss of vision was present, and there was a complete optic atrophy. All of these patients had dilated pupils. Myosis is a common symptom in adults with tabes; in the young, dilatation of the pupil seems much more common. In cases 1 and 3 the pupils were unequal, and in case 2 they were slightly irregular. Complete pupillary rigidity, the so-called frozen pupil, was present in all three cases. Some observers have mentioned the occurrence of the Argyll Robertson pupil as also occurring in juvenile tabes. As already mentioned, in all these cases the patients had frozen pupils, and I have not observed the Argyll Robertson pupil in any other form of cerebrospinal syphilis in children. The patient in case 3 had a convergent squint. In case 1, the patient had a divergent squint, and he was the only one of the three who had nystagmus; this was of the ocular type. Ptosis was not found in any of these patients.

Hearing was good in each of the three cases, and there was no weakness of any of the other cranial nerves.

None of my patients had symptoms referable to the bladder. In his survey of the recorded cases, Fairbanks [9] found these symptoms the second most frequent of the initial symptoms.

As far as I was able to determine, none of these patients had any cutaneous sensory disturbances. It is difficult in young children, however, to be certain that they are correctly distinguishing pain, sensation of touch, heat and cold.

Gastric crises were present in two of the cases (cases 2 and 3). Crises in a given case are apt to recur at more or less regular intervals and to be similarly severe when they recur. Thus the patient in case 3 had excruciatingly painful crises every few months, and vomiting was severe; the patient in case 2 had much less pain, and the periods were much more frequent, recurring every week or two, and the vomiting was not so severe as in the former case. Gastric crises are among the rare manifestations of juvenile tabes dorsalis. Fairbanks [10] mentions, however, that viceral crises were the initial symptoms in two cases of children, aged 6 and 11 years.

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8. Church, A.: Diseases of the Nervous System, p. 492.
9. Fairbanks, Arthur W., in Abt's Pediatrics, 1925, vol. 7, p. 608.
10. Fairbanks, Arthur W., in Abt's Pediatrics, 1925, vol. 7, p. 609.

These children all seemed bright, and there was no mental disturbance. The patient in case 3 read easily and talked remarkably intelligently at the age of 7. The patient in case 2 played between attacks and talked normally. The patient in case 1, who is blind, knows the voices of the nurses and the physicians at the clinic and always converses intelligently with each person whom he knows.

Because of the paucity of reported cases of juvenile tabes, three cases are reported with comments.

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Progress in Pediatrics

ENDOCRINE GLANDS IN RELATION TO INFANCY AND CHILDHOOD *

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If it is true that some of the disease syndromes of infancy and childhood owe their origin to either excess or deficiency of certain of the incretions; if it is true that the several metabolic processes as well as the activities of the vegetative nervous system are subject to regulation by substances of endocrine origin; if it is true that physical and mental growth and development in early life are, in a large measure, influenced by the chemical products of the ductless glands, and if it is true that human constitutions differ markedly in their incretoglandular make-up, then surely every pediatrician should be interested in endocrinology and its progress.

My subject is, I admit, a somewhat dangerous one. Though the field of endocrinologic facts is already wide and important, that of endocrinologic fancy is altogether too fascinating. The latter province has, in some quarters at least, undergone harmful over-exploitation; the big balloon of endocrine "hot air" is, I feel sure, certain soon to be subjected to drastic deflation. None the less, the opportunities for the expansion of the actual knowledge in endocrine domains are most attractive, and an army of workers is busy in seizing them. Real progress, all will agree, is being made, despite much pseudoprogress that is illusory. And even error, as medical history has manifoldly proved, may be useful in that it often stimulates controversy that leads to new inquiries from which new truths emerge.

SYNDROMES OF ENDOCRINE ORIGIN THAT INTEREST PEDIATRICIANS

If one studies the evolution of medical thought one can scarcely escape the conviction that it has been the astute and closely observant clinician who has led the way in the making of a large number of the new paths to medical knowledge. This would seem to be particularly true of the endocrinologic pathways, for it was the recognition and accurate description of certain classic complexes of symptoms that marked the entrances to the routes that were followed by pioneers in

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* Read by invitation before the New York Academy of Medicine, Section of Pediatrics, Jan. 12, 1928.

the investigation of the functions of the ductless glands. When one thinks of the thyroid gland, one's mind reverts to the syndromes described by Flajani (1800), Parry (1825), Graves (1838), Basedow (1840) and Marie (1883) on the one hand, and to those pictured by Norris (1847), Curling (1850), Hilton Fagge (1871), Gull (1874), Ord (1880), Reverdin (1882), Kocher (1883), Semon (1883) and Horsley (1885), on the other. When one thinks of the pituitary gland, one recalls the clinical observations of Marie (1886) on acromegaly and those of B. Mohr (1840) and of Fröhlich (1901) on the condition now known as dystrophia adiposogenitalis. Similarly, when one thinks of the parathyroid glands, one must realize that the road to knowledge of their functions was first opened by European clinicians—Clarke (1815) and Kellie (1816) in Great Britain; Steinheim (1830) in Germany, and Dance (1831), Tonnelle (1832) and Corvisart (1852) in France—who described the clinical syndrome now known as tetany, long before the parathyroid glands were found by Sandström (1880) and before the physiologist Gley discovered their physiologic significance by experiment on animals. If it were necessary, I could also adduce evidence from medical history that the establishment of definite clinical syndromes—Addison's symptom-complex, pseudohermaphroditism, premature puberty and hirsutism with virilism for the suprarenal, eunuchism and eunuchoidism for the gonads, and diabetes mellitus for the islands of Langerhans—formed the adits to the long channels of research that have resulted in the present knowledge of still other glands of internal secretion. No matter how important the contributions of anatomists, physiologists, biochemists, pathologic histologists and pharmacologists to this division of medical science, clinicians will always have reason for pride in having thus led the way in endocrinology; this pride should stimulate to ever closer and more discriminating observation of patients in the hope that still finer analysis followed by sagacious synthesis must sooner or later open the door not only to further enrichment of syndromology, but through the heuristic effect of the latter, to important advances in the knowledge of pathogenesis.

Thyreopathic Syndromes in Childhood.—Though hyperthyroidism is rare in childhood, the child specialist should be on the lookout for it, since exophthalmic goiter has been reported as occurring as early as the third year of life; in a number of instances, it has been discovered between the ages of 3 and 10 years. Besides the cardinal symptoms of vascular goiter—prominence of the eyes, tachycardia and fine tremor of the fingers—the symptoms that should be kept in mind as possibly due to it include rapid emaciation without apparent cause, excessive sweating, bulimia, unmotivated watery diarrhea, emotional instability, mental over-

alertness and physical restlessness. In such cases, the determination of an accelerated basal metabolic rate may be decisive for the diagnosis in the absence of the Mersenburger triad. Fortunately, at this early age, hyperthyroidism (or dysthyroidism) may often be corrected by correcting faulty hygiene and by the temporary use of soothing remedies (bromides, phenobarbital), though in exceptional cases thyroidectomy (after a few days' preparation by iodine medication) may be necessary even in childhood.

In early life, hypothyroidism is much more common than hyperthyroidism. There can scarcely be any practitioner who has not had opportunity to become familiar with the clinical syndromes of cretinism and of "childhood myxedema." The slowed mental and physical development, the drowsiness or lethargy, the tendency to obesity, the thick, coarse wrinkled skin, the open, drooling mouth with cyanotic lips and enlarged tongue, the scanty, lusterless hair, the sunken eyes with narrow lidslits, the plump hands with short fingers, the pot belly with umbilical hernia, and the obstinate constipation are characteristic, even in early childhood; whereas, a little later, the persistent dwarfism, the delayed dentition, the failure of the ossification centers to develop properly, and the retarded basal metabolic rate are additional criteria of importance. In many of these patients, the effects of substitution therapy (thyroid feeding) are fortunately often gratifying. In the severer forms of cretinism or of thyroaplasia, transplantation of a piece of exophthalmic thyroid (the end of the superior thyroid artery of the transplant being sutured into the common carotid artery of the receiver) may be justifiable, as Bagoras has recently demonstrated.[1]

The beneficent effects of minimal doses of iodine for the prevention of colloid goiter in school children are, of course, fresh in the minds of all. Marine and Kimball[2] made a most important contribution to prophylaxis when they showed how to prevent the development of this form of goiter in regions in which it is endemic. A note of warning, however, should perhaps be sounded against the indiscriminate use of iodine tablets or of iodized salts without strict medical supervision and control.

Parathyreopathic Syndromes in Childhood.—The recognition that tetany can be the result of deficiency of parathyroid function has greatly stimulated the interest of pediatricians in endocrinology. The main steps in establishing the relations of hypoparathyroidism to tetany were the early observation of Weiss that tetany occurred sometimes after removal of a goiter (tetania strumipriva); the discovery of the minute parathy-

1. Bagoras: Zentralbl. f. Chir. **53**:3156, 1926.

2. Marine, David, and Kimball, O. P.: Prevention of Simple Goiter in Man, Arch. Int. Med. **22**:41 (July) 1918.

roid glands embedded in the thyroid by Sandström; the fact established by Gley (1890) that when the thyroid and parathyroids are simultaneously extirpated in rabbits tetany occurs, though not when the thyroid alone is removed, and the conception of Vassale and Generali (1896-1897) that in man, after strumectomy, if tetany appears, it is because of removal of, or injury to, the parathyroids, whereas, if parathyroid function is preserved, tetany does not occur though myxedema may appear.

The clinical syndrome of manifest tetany, characterized by spontaneous attacks of intermittent tonic contractions in groups of special muscles (carpopedal spasm, laryngospasm, facial spasm, etc.), led gradually to careful studies of children who exhibited the so-called spasmophile diathesis. As a result, clinicians learned how to recognize latent tetany by means of the signs of Trousseau, of Chvostek and of Poole, above all by testing for increased galvanic excitability of the motor nerves (Erb's sign); they also learned that in chronic tetany in children peculiar trophic disturbances are often recognizable, especially parallel rows of defects of the enamel of the teeth and bilateral perinuclear opacity of the crystalline lens. Another fact of fundamental importance was the discovery of a diminution of the calcium content of the blood in different forms of tetany as well as the beneficial effects of the administration of calcium in combating both the hypocalcemia and the hyperexcitability of the nervous system.

There is still some doubt as to whether every case of tetany is due to hypoparathyroidism and, recently, many studies of experimental bicarbonate tetany and hyperventilation tetany have been undertaken. However, that most tetany in man is parathyreogenous would seem now to have been firmly established. One of the strongest evidences of this lies in the abolition of the syndrome of tetany in animals after parathyroidectomy and of the symptoms of spontaneous human tetany through administration of a really potent parathyroid extract (parathyroid extract-Collip [3]). In a dog weighing 20 Kg., 100 units of this extract will raise the calcium level in the serum by 5 mg. per cent after fifteen hours. Several children with tetany have been treated by Collip, by Petty, Stoner and Schaffer, by Hoag and Rivkin [4] and by others. In a number of instances, the patients were promptly relieved by a dosage of 5 units of extract per kilogram of suckling weight, given at intervals of from four to six hours for a few doses. The symptoms of tetany

3. Collip, J. B.: Therapeutic Value of Parathyroid Hormone, Medicine **5**:1, 1926; Calcium Mobilizing Hormone of Parathyroid Glands, J. A. M. A. **87**:908 (Sept. 18) 1926; ibid. **88**:565 (Feb. 19) 1927.

4. Hoag, L. A., and Rivkin, H.: Treatment of Infantile Tetany with Parathyroid Extract, J. A. M. A. **86**:1343 (May 1) 1926.

usually disappeared when the level of the blood calcium reached 9 or 10 mg. per hundred cubic centimeters. Similar results have been obtained in chronic tetany by John.[5] Even in experimental bicarbonate tetany, in which there is a diminution of calcium ions in the blood, the onset of the tetany can be delayed, as has been shown by Holt, Stregel and Perlzweig,[6] by producing a hypercalcemia with parathyroid extract before the bicarbonate was administered.

But there are many problems in the tetany of childhood still to be solved. It is not yet certain that all tetany is of hypoparathyroid origin; moreover, the cases of marked hypocalcemia without tetany still remain to be explained. Further, the relations of other disturbances of electrolyte equilibrium as well as of the guanidine or methyl-guanidine content and the vitamin content of the blood to tetany require further study. Nevertheless, Collip's isolation of a potent parathyroid extract that can quickly raise the calcium content of the blood temporarily marks an important advance.

Whether or not a clinical syndrome due to hyperparathyroidism occurs in man is not yet certain. Theoretically, such a syndrome is conceivable. In dogs, as Collip has shown, large doses of parathyroid extract-Collip may produce a hypercalcemia with vomiting, drowsiness, pallor, atony and circulatory failure, an intoxication against which a 25 per cent solution of dextrose seemed to be of value as an antidote.[7] Students of disease in children would do well, I think, to be on the lookout for such a syndrome.

Hypophyseopathic Syndromes in Childhood.—Three principal clinical syndromes in childhood have been associated with disorders of the pituitary gland or the hypophysis cerebri: (1) gigantism and acromegaly (supposedly due to overactivity of the anterior lobe); (2) dwarfism and dystrophia adiposogenitalis (due to underactivity of the anterior lobe), and (3) diabetes insipidus (due to underactivity of the pars intermedia and pars posterior). It is a fact that true acromegaly occurs rarely in childhood, though a few cases have been described; gigantism, however, occurs frequently at an early age, and Fröhlich's syndrome (with acromicria, hypoplastic genitalia and obesity) is relatively common. In many of these cases, roentgenograms of the sella turcica, charts of the visual fields showing bitemporal visual defects and the signs of increased intracranial pressure point to enlargement of the hypophysis due to neoplasm or to hypophyseal struma. Diabetes insipidus, too, is not infrequently encountered in children and

5. John: Ann. Surg. **85**:410, 1927.

6. Holt, Stregel and Perlzweig: Monatschr. f. Kinderh. **34**:437, 1926.

7. Collip: Am. J. Physiol. **76**:472, 1926.

has been supposed to be due to a lowering of the renal threshold for excretion of water because of insufficient production of pituitary.[8]

Attacks on the hypophysis for the removal of tumors and other involvements have led to the development of a new field in surgery and, in some cases of deficiency of hypophyseal function, substitution therapy with whole gland or with extracts of the different lobes has met with some success. These and other methods of therapy (radiation) are as yet, however, far from satisfactory in the hypophyseal diseases, though it is to be hoped that in time it may become possible to achieve results hitherto beyond reach.

The whole matter of hypophyseal syndromes has recently been complicated by advances in knowledge of the functions of parts of the brain, especially of the tuber cinereum and the infundibulum, which (like the posterior lobe of the hypophysis) are parts of the pars optica hypothalami of the diencephalon.[9] Experiments on animals and studies of the brains of patients who have died of epidemic encephalitis have revealed the fact that lesions of the tuber can give rise to clinical syndromes apparently identical with the principal hypophyseal syndromes. From now on, when these syndromes are encountered, the question must be asked, Are they due to disease of the hypophysis itself or to disturbances in the immediately adjacent hypothalamus? The answer may be difficult, since an enlarging hypophysis may easily injure its next door neighbor, the tuber cinereum!

Thymopathic Syndromes in Childhood.—Regarding the endocrine functions of the thymus, there has been much dispute, but that certain clinical syndromes are associated with abnormalities of the thymus, there can be no doubt.[10] Among the clinical phenomena most often observed when marked thymic enlargement is present are attacks in which a child, on crying, holds its breath, turns blue and temporarily loses consciousness (asphyxiation seizures). In some children there may be simple syncopal attacks, persistent cyanosis, coughing spells, choking spells, snorting respiration or asthmatic attacks. Some believe that these phenomena are due to pressure; others that they are due to thymic intoxication. Roentgen rays are important, not only for diagnosis but

8. Barker, Lewellys F. and others: Endocrinology and Metabolism, New York, D. Appleton & Company, 1922, vol. 1, pp. 706-924; see also Tilney, F.: Contribution to the Study of the Hypophysis Cerebri, Philadelphia, 1911, and Cushing, Harvey: The Pituitary Gland and Its Disorders, Philadelphia, J. B. Lippincott Co., 1921.

9. A recent review of this subject is that of Cloake, T.: The Influence of the Diencephalon ('Tween Brain) on Metabolism, Proc. Roy. Soc. Med. (Sect. Neurol.) **20**:1643, 1927.

10. Compare Cowdry, Hoskins, Crotti and Hoxie: The Thymus Gland and Its Diseases, in Endocrinology and Metabolism, p. 361.

for treatment, as the size of the thymus (and probably also its functional activity) can be speedily reduced by appropriate radiation.[11]

The recognition of the status thymicolymphaticus is important because of the danger of sudden death (mors thymica). In addition to enlargement of the thymus, the existence of a marked lymphocytosis in the blood and the presence of very large medial and very small lateral incisor teeth in the upper jaw are clues to diagnosis. It has been suggested by MacLean and Sullivan[12] that the sudden deaths in status thymicolymphaticus may be related to disturbances of the regulation of blood sugar.

Recently, the importance of the function of the thymus for the development of the genital organs has been stressed by French clinicians. The subject would seem worthy of further inquiry.[13]

Suprarenalopathic Syndromes in Childhood.—The suprarenalopathic syndromes in childhood may depend on involvement of the chromaffin part of the suprarenal body, of the cortical (or interrenal) part, or of both.

Addison's disease with its asthenia, low blood pressure and pigmentation of the skin and mucous membranes is rarely, though occasionally, encountered in childhood.[13a]

Syndromes attributed to hyperplasias or to neoplasms of the cortex of the suprarenals are, however, among the most remarkable pictures encountered in clinics for children; I refer, of course, to pseudohermaphrodism and to premature puberty.

Time will not permit me to enter on a discussion of the theories regarding the origin of these syndromes, but any one who is especially interested will enjoy reading the recent papers of Schwarz.[14]

Syndromes of Gonadal Origin in Childhood.—The similarity of the bodily and mental development in so-called eunuchoidism to that observable in true eunuchs makes it seem certain that the eunuchoid phenomena so often seen in boys with undescended testicles depend on a deficiency of the internal secretion of the sex glands (gonads). The failure of the secondary sex characters (hair, voice, psyche) to develop normally is a striking feature, as is the roentgenographic demonstration in the bones of the failure of the closure of the epiphyseal junctures.

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11. Compare also Morgan, E. A.; Rolph, A. H., and Brown, A.: Clinical Manifestations of an Enlarged Thymus, J. A. M. A. **88**:703 (March 5) 1927.

12. MacLean and Sullivan: Proc. Soc. Exper. Biol. & Med. **23**:753, 1926

13. Compare Mandelstamm, M.: De l'action possible du thymus sur les organes génitaux, Paris, 1927, p. 47.

13a. Compare Cohoe, B. A.: Addison's Disease, in Endocrinology and Metabolism, vol. 2, p. 277.

14. Schwarz, E.: Zwischenniere und Zwittertum, Wien. klin. Wchnschr. **14**: 140; 213; 257, 1927.

The clinical picture of hypogenitalism in the female (hypovaria) is less cleancut than that in the male (hyporchia), particularly in the young. The possible relations of these hypogenital syndromes to underactivity of the hypophysis, the suprarenal cortex or the thymus have already been hinted at; but as yet too little is known to permit of positive statements. Moreover, a satisfactory therapy for these conditions still remains to be worked out.

Insulopathic Syndromes in Childhood.—The proof that diabetes mellitus (with its glycosuria, hyperglycemia and dangers of ketosis) depends on deficiency of the autacoid substance manufactured by the islands of Langerhans of the pancreas (hypoinsulinism) and the simplification of treatment by means of the insulin isolated by Banting and his associates are among the greatest of the triumphs of the medicine of the present time. The amount of research in progress in this field is appalling. I shall not attempt even to refer to the newer studies, for good collective reviews are everywhere available.[15] It is a cause for especial gratification that diabetes in childhood, formerly so malign, can now be kept under control with insulin if it is properly applied.[16]

In the treatment of diabetic persons with insulin, hypoglycemia may easily develop unless great caution is exercised. Clinicians have therefore had manifold opportunity to become familiar with an accidentally induced insulinic hypoglycemic shock syndrome that was new to them and was characterized by convulsive seizures or by transient loss of consciousness. Reports of this condition in children are not lacking in medical literature.[17] An acquaintance with this syndrome and with the methods of treating patients in whom it is present, as well as with methods of preventing it, is desirable for every physician who undertakes the management of diabetic patients.[18] Since the recognition of hypoglycemia thus induced by injections of insulin, physicians have been on the alert to see whether clinical syndromes due to spontaneous hypoglycemia (and perhaps to a pathologic hyperinsulinopathy) did not occur. Already they have been rewarded by finding the syndromes in adults. Thus, at the Mayo Clinic, Wilder[19] and his associates have

15. Compare especially Macleod, J. J. R.: Carbohydrate Metabolism and Insulin, New York, Longmans, Green & Company, 1926, p. 357; Joslin, E. P.: Treatment of Diabetes Mellitus, latest edition, Philadelphia, Lea Brothers.

16. Compare Joslin, E. P.: End Results in Treatment of Diabetes Mellitus in Children, J. A. M. A. **88**:28 (Jan. 1) 1927. Priesel, R., and Wagner, R.: Insulin Needs of Diabetic Children, Monatschr. f. Kinderh. **34**:498, 1926.

17. Compare Harrison, G. A.: Brit. M. J. **2**:57, 1926.

18. Compare Best, C. H.: Laboratory Aspects of the Problem of Diabetes, Ann. Clin. Med. **5**:1081, 1927. Harrop, G. A., Jr.: Hypoglycemia and Toxic Effects of Insulin, Arch. Int. Med. **40**:216 (Aug.) 1927.

19. Wilder, R. M., et al.: Carcinoma of the Islands of the Pancreas, J. A. M. A. **89**:348 (July 30) 1927.

described a case in which hyperinsulinism and hypoglycemia were due to carcinoma of the islands of Langerhans; and, in my own clinic, Drs. Sprunt and Trescher have made careful studies of the blood sugar of a patient who exhibited frequent spontaneous hypoglycemic crises, which they attributed to hyperfunction of the islands (hyperinsulinism). At Dr. Sprunt's request, Dr. Finney resected the pancreas of this patient, removing especially the part of the organ in which the islands are most abundant; the operation has been followed by a definite diminution of the hypoglycemic tendency and by a marked amelioration of the symptoms.[20] It is not improbable that similar syndromes will before long be encountered in children, if they are closely watched for.

One group of hyperglycemic cases that has aroused clinical wonder lately should be mentioned, namely, that group in which reduction of the increase in blood sugar is refractory to treatment with insulin. Such insulin-resistant syndromes have been found in certain infections,[21] in certain neuropathic states [22] and in association with still other conditions. The cause of the refractoriness is not yet entirely clear in all instances. In this connection, the observations now being made on the antagonism of glycemin,[23] epinephrine,[24] and of pituitary [25] to insulin may prove to be illuminating.

AUTACOID SUBSTANCES USED AS PHARMAKA

Since the isolation of thyroxin, epinephrine, pituitary, parathyroid extract-Collip and insulin, there has been evident an ever increasing tendency to make use of these substances as pharmaka in various states in which it is desired to influence pathologic-physiologic mechanisms. I need refer only to the use of: thyroxin for the acceleration of carbohydrate, protein and mineral metabolism in certain diseases other than those due to hypothyroidism;[26] epinephrine for vasoconstriction of vascular tissues, for the favoring of sympathetic innervations of various sorts, for resuscitation of the heart in syncope by intracardiac injection, and, above all, for the relief of bronchospasm in asthmatic states; pituitary for portpartum hemorrhage, for increasing the concentration of the urine in excessive diuresis and for overcoming postoperative intestinal atony; parathyroid extract-Collip for influencing the mobilization

20. Later on this case will be reported in full by Drs. Sprunt and Trescher.

21. Brit. J. Exper. Path. **8**:58, 1927.

22. Bull. et mém. Soc. méd. d. hôp. de Paris **51**:993, 1927.

23. Klin. Wchnschr. **6**:8561, 1927.

24. Biochem. Ztschr. **183**:283, 1927; Arch. f. exper. Path. u. Pharmakol. **121**: 299, 1927.

25. Edinburgh M. J. **34**:343, 1927.

26. Compare Boothby, Sandford et al.: Arch. d. mal. de l'app. digestif **17**: 481, 1927.

and utilization of calcium not only in tetany, but in the faulty coagulability of the blood in jaundice, in promoting formation of callus after fracture, in soothing the nervous system in epilepsy, etc.,[27] and of insulin for the promotion of gain in weight of emaciated and cachectic children, for lessening the physiologic loss of weight in the new-born child, especially after premature delivery, for preventing too great loss of water in infantile vomiting or diarrhea and for combating traumatic or postoperative shock (then given in combination with dextrose).[28] Though these new substances are important additions to pharmacotherapeutic resources, great care should be taken not to abuse them; they are powerful agents, capable of producing reactions that are not devoid of danger unless the dosage is most carefully adjusted.

RELATION OF ENDOCRINE STUDIES TO STUDIES OF PSYCHOPHYSICAL CONSTITUTION

With the marked revival of studies of constitution during the past few years, much attention has been paid to the part played by the incretory glands in the development of the psyche and the physique of human organisms; in other words, to the relation of the endocrine glands to what is known as "constitution" and "constitutional disposition."[29] The materials derived from the two parents to form the fertilized egg cell from which each individual develops determine the possibilities of development; what actually does develop depends on reactions of the materials of parental origin with environmental substances and influences.[30] The realized person (or phenotype) is then a psychophysical organism that has resulted from a series of reactions of a genotypic

27. Hoag, L. A., et al.: Effect of Potent Parathyroid Extract on Calcium Balance in Infants, Am. J. Dis. Child. **33**:910 (June) 1927. Lehman, E. P., and Cole, W. H.: Parathyroid Hormone and the Calcification of Fracture Callus, J. A. M. A. **89**:587 (Aug. 20) 1927. Hueper, Wilhelm: Effect of Repeated Injections of Parathyroid Extract on Calcification of Osteoid Tissues, Arch. Path. **3**:1002 (June) 1927. Davidson, C. F.: Northwest Med. **26**:181, 1927.

28. Stolte, K.: On the Question of Insulin Treatment in Nondiabetic Children, Therap. d. Gegenw. **68**:64, 1927. Spickard, V. W.: Use of Insulin in the Treatment of Certain Nondiabetic Conditions of Infancy and Childhood, Northwest Med. **26**:282, 1927. Randall, H. E.: Traumatic Shock, J. Michigan M. Soc. **26**: 19, 1927. Anderson, C. M.: Use of Glucose and Insulin in Prevention of Surgical Shock, California & West. Med. **27**:56, 1927.

29. Draper, G.: Human Constitution, Philadelphia, W. B. Saunders Company, 1924. Bauer, J.: Die konstitutionelle Disposition zu inneren Krankheiten, ed. 3, Berlin, J. Springer, 1924. Josefson, A.: Die Persönlichkeit und die Einsonderungsorgane ("endokrine Drüsen"), in Die Biologie der Person (Brugsch-Lewy), Berlin, Urban & Schwarzenberg, 1927, vol. 3, pp. 103-126.

30. Draper, G.: Heredity and Environment—the Disease Makers, Am. J. M. Sc. **171**:803, 1926.

pattern with its surroundings; the "determination factors" are in the genotype, whereas the "realization factors" are in the environment (Roux).

During growth and development, the parts of the organism are correlated, partly through nervous influences, partly through chemical (hormonal) influences. It should not be forgotten, however, that the nervous system and the incretory system are themselves just as much genotypically determined as are the other systems of the body that they influence; they are also dependent for their growth and development on realization factors of the environment, as are all other parts. Each cell of the body has its own inherent developmental impulses, and these autochthonous urges in each cell are subjected, in greater or less degree, to trophic nervous influences, on the one hand, and to direct physical and chemical influences that impinge on them, on the other. In studying human beings, then, in regard to their "constitutions" or "psychophysical make-up," one must consider both the inherited factors and the environmental factors. For a given physical habitus or for a given psychic trend, the origin must be sought in one set of factors, in the other set, or in both. "Constitution clinics" are evidently aware of the profound significance of the endocrine glands for both physical features and mental tendencies; in persons of dysplastic habitus, especially, incretory imbalance is often held responsible, and such imbalance may have resulted either from gametic influences or from injury (prenatal or postnatal). Lucky is the person born and reared with an optimal incretory apparatus!

Possibly studies of the actual weight relations of the different endocrine glands of the children who die during the five different periods of growth now distinguished by pediatricians will give clues for the differences in persons as regards the endocrine formula corresponding to each period. Hitherto there has been much talk but little actual work on "endocrine formulas," but recent studies of constitution made by Russian students are more objective and are to be welcomed.[31]

The mechanism of transmission of genotypic trends has been the object of intensive biologic study in the present time;[32] though progress in the study of the fruit fly has been greater than in the study of man, still one has good reason to be pleased with the light that recent studies of human inheritance have thrown on the reciprocal relations of con-

31. Fertik, I. M.; Majanz, A. I., and Monossohn, S. M.: Ueber die endocrinologische Formel bei Kindern in verschiedenen Altersperioden, Jahrb. f. Kinderh. **115**:363, 1927.

32. Conklin, E. G.: Heredity and Environment in the Development of Men, ed. 2, Princeton, 1916. Davenport, C. B.: Heredity in Relation to Eugenics, New York, 1911.

stitution and single endocrine functions.[33] Students of constitution now speak of the hypothyreotic constitution, of the thyreotoxic constitution, of hereditary and familial parathyreosis, of hypophyseopathic constitutions, and of the like; they are directing attention in increasing degree to familial trends; for example, to the occurrence of exophthalmic goiter and diabetes or obesity in certain families, to the alternation of acromegaly and myxedema in other families, or to the variety of endocrinopathies that may be encountered in the descendants of persons who have suffered from exophthalmic goiter. Since the earlier the tendencies of persons to pathologic states are discovered the greater the possibility of beneficial intervention by means of corrective exogenous influences, a great responsibility obviously falls on the shoulders of the child specialist.

Though such attention to the significance of the genotype is important, it must not be forgotten that faulty heredity is sometimes blamed when prenatal or early postnatal injuries [34] are in reality culpable. The velocity of growth and development seems to stand in intimate relation to certain incretory influences. Even during intra-uterine life, the amount and character of increta reaching the fetus from the mother may be of import for early processes of differentiation.[35] The profound effects observed by Gudernatsch, Hart, Crew, Hoskins, Lawrence, Uhlenhuth, Pearl, Schäfer and others, who fed thyroid, thymus, hypophysis, suprarenal cortex, and ovary to frogs' larvae, chicks, white rats, etc., make one aware that one dare not lose sight of the possibility of analogous influences during human embryonic life. Injuries to the human fetus due to congenital syphilis exert their harmful influence, in part at least, through involvement of the endocrine functions.[36] Constitution is not a fixed thing; it changes from age period to age period, from year to year, indeed, at least minimally, from hour to hour, as the inherited materials interact with the environment, especially during growth and development. Experiments with chemicals and with the roentgen rays on young animals may profoundly disturb development in either form or rate. Methods must be worked out that will permit a more accurate determination than is now possible of the criteria for the distinguishing of both "types" and "constitutions" and for the recognition of the disease predispositions that these entail.[36] If

33. Huxley, J.: Ductless Glands and Development, J. Hered. **13**:349, 1922; **14**:3, 1923.

34. Pugliese, A.: Arch. ital. de biol. **50**:1, 1920.

35. Valkema Blouw, H. C.: Tijdschr. v. Geneesk. **68**:1039, 1924.

36. Hutinel, V., and Stévenin, H.: Syphilis héréditaire et dystrophies (aperçu de pathologie générale infantile), Arch. de méd. d. enf. **23**:5, 1920.

36. Cf. Stockard, C. R.: Constitution and Type in Relation to Disease. Bagg, H. J., and Little, C. C.: Hereditary Structural Defects in the Descendants of Mice Exposed to Roentgen-Ray Irradiation, Am. J. Anat. **33**:119, 1924.

physicians desire to extend their power to understand, to predict and to control the biologic functions of single persons, they should do all in their power to foster the study of the really fundamental principles and the development of the practical technical methods of both eugenics and euthenics. There cannot be any doubt that, as such studies grow, the ductless glands and the autacoid substances they produce will receive their due share of attention; that this share will be a large one seems to be certain, unless the glimmerings of truth we now think we have are leading us wholly astray.

THE HYPERTROPHIES OF INFANCY AND CHILDHOOD *

A. V. STOESSER, M.D.
MINNEAPOLIS

An abnormal swelling or enlargement of one or more extremities, of certain portions of the body, or of one half of the body has always been considered an interesting condition. Often the determination of the exact nature of the hypertrophy is difficult, especially in the first and second decades of life. In addition, the prognosis and the treatment present a problem the solution of which is still more difficult. In view of this, an attempt has been made to develop a classification of the hypertrophies of infancy and childhood, based on a few cases, one of which is reported in detail, together with a review of the literature.

The following classification is presented at this time with the hope that it will be of some value in the diagnosis, and possibly in the prognosis and the treatment.

CLASSIFICATION

I. True hypertrophy (macrosomia or gigantism)
   A. Congenital
      1. Partial hypertrophy
         (*a*) Hemihypertrophy
         (*b*) Crossed type of hypertrophy
      2. Total hemihypertrophy
   B. Acquired
II. False hypertrophy
   A. Congenital
      1. Milroy's disease (congenital or hereditary edema)
      2. Elephantiasis
      3. Hemihypertrophy
   B. Acquired (elephantiasis)

The true hypertrophies (see classification) include conditions in which there is a variable hypertrophy of the soft tissues together with an enlargement of the muscles and also an increase in size of the underlying bone. If the condition is noticed at or soon after birth, it may be considered as congenital in origin. The enlargement may involve one or more extremities or certain other parts of the body, and in either case it is to be classified as a partial hypertrophy of the true type. If the condition is confined to one side of the body, it is a partial hemihypertrophy of the true type. Often these hypertrophies have been described

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in the literature under the name of macrosomia. In 1920, Black-Milne [1] reported two cases in boys aged 18 years; in one, the right arm and leg were larger in circumference and longer than the extremities of the left side. In addition, there was an increase in size of the right side of the head, the chest and the abdomen. In the second patient, the right leg was definitely longer than the left. Horwitt [2] described this condition in a girl, aged 5 months, who had had a hypertrophy of the left lower extremity since birth. Edema was not present except for a small amount over the dorsum of the foot. The roentgenogram showed the bones of the left extremity to be larger than those of the right. In 1926, Fenner [3] presented a case which is a striking example of a partial congenital hemihypertrophy of the true type. His patient, a girl, aged 7 years, presented a left lower extremity 5 inches (12.7 cm.) longer than normal, and twice the circumference of the right, especially below the knee. The skin of the hypertrophied extremity was rough and the bones increased in size. It appears from reported cases that partial congenital hemihypertrophy of the true type usually involves only certain portions of the body, such as an arm, a leg, or even only a toe or a digit. The condition is noticed at or soon after birth. The skin is usually smooth, although it may be rough and thickened, approaching the appearance of that seen in elephantiasis. Pigmentation of the skin, nevi and telangiectases may be present. Pitting is not a characteristic feature of the disease. The subcutaneous tissue, the muscles and the bones are involved, the latter involvement being important and essential. The increase in size of the bones produces a lengthening of the affected extremity or extremities.

In some instances of partial hypertrophy of the true type, the hypertrophy is not unilateral but is crossed, so that, for example, an arm on one side of the body, and a leg on the other side of the body are involved. The condition is then classified as a partial congenital true hypertrophy of the crossed type. Gesell [4] collected reports of thirty cases of partial hypertrophy, six of which were of the crossed type.

If the hypertrophy covers practically one entire half of the body, it is called a total congenital hemihypertrophy of the true type provided an enlargement of the bones is present. A review of the literature reveals many case reports. In 1916, Hutchison [5] reported the case of a

1. Black-Milne, J.: Two Cases of Anomalies of Growth, Brit. J. Child. Dis. **17**:79, 1920.

2. Horwitt, S.: Congenital Macrosomia, Arch. Pediat. **43**:67 (Jan.) 1926.

3. Fenner, E. D.: Macrosomia or Congenital Hypertrophy, M. J. & Record **123**:501 (April 21) 1926.

4. Gesell, A.: Hemihypertrophy, Arch. Neurol. & Psychiat. **6**:400 (Oct.) 1921.

5. Hutchison, R.: A Case of Hemi-Hypertrophy with Post-Mortem Examination, Brit. J. Child. Dis. **13**:233, 1916.

boy, aged 5 months, in whom there was an abnormal increase in the circumference and the length of the right arm and leg together with an enlargement of the chest, the abdomen and the testicle on the same side. He considered this condition a hemihypertrophy for when the case came to autopsy, the internal organs of the right side, especially the suprarenal, were larger than normal. Hall [6] observed a girl, aged 7 months, whose body had been larger on one side than on the other since birth. The right cheek, the right ear and the right side of the tongue were larger than they were on the left side. There was a pendulous sagging of the abdomen on the right side, and the right labium majus was large. The right arm was longer than the left, but the right leg was greater in circumference and was longer than the left. Paterson and Reynolds [7] reported two cases, in one of which a girl, aged 6 months, had an enlargement of the left side, involving the cheek, the ear, the breast, the thoracic musculature and also the lower extremity. The roentgenogram revealed thickening and hypertrophy of the bones of the left lower extremity. Stanton and Tuft [8] presented a case in 1923. Mayers [9] reported a case in a girl, aged 9 years, who since birth has shown enlargement of the right half of her body, involving the soft tissues, the muscles and the bones. In 1926, Lenstrup [10] published a report concerning eight patients with hemihypertrophy observed during the last twenty years at the Queen Louise's Children's Hospital in Copenhagen. Only three of these can be considered as having true hemihypertrophy, for in only three did roentgen-ray examination reveal involvement of the bones.

The cause of the hypertrophies of the true type undoubtedly is not conclusively established at the present time. The opinion of Gesell, who collected reports of forty cases of hemihypertrophy, is interesting and as stated by him is as follows:

> In a discussion of the etiologic theories for hemihypertrophy preference is given to the view that hemihypertrophy is not a hereditary character, but a morphogenetic anomaly dating back to an early embryonic stage.
>
> Hemihypertrophy is interpreted as a form of asymmetry due to a possible deviation in the normal process of twinning.

As to the progress of the condition with advancing age, Lockhart-Mummery [11] observed a patient with hemihypertrophy for eighteen and

6. Hall, E. G.: A Case of Hemi-Hypertrophy, Brit. J. Child. Dis. **18**:21, 1921.

7. Paterson, D., and Reynolds, F. N.: Two Cases of Congenital Hemi-Hypertrophy, Lancet **1**:23 (Jan. 6) 1923.

8. Stanton, J. N., and Tuft, L.: Congenital Total Hemihypertrophy, J. A. M. A. **80**:1432 (May 19) 1923.

9. Mayers, L. N.: Hemihypertrophy, Surg. Gynec. Obst. **43**:746 (Dec.) 1926.

10. Lenstrup, E.: Eight Cases of Hemihypertrophy, Acta Paediat. **6**:205, 1926.

11. Lockhart-Mummery, J. P.: Case of Hemi-Hypertrophy Traced for Eighteen and a Half Years, Proc. Roy. Soc. Med. **17**:1 (Jan.) 1924.

one-half years. At the age of 2½ years, the left leg was 1½ inches (4 cm.) longer than the right, while at 4½ years it had increased to 3½ inches (9 cm.). At 21 years, however, the difference had practically disappeared, there being only a half inch difference in length between the two lower extremities. Lenstrup also was able to follow some of his cases for a long time (from five to nineteen years) and observed that during childhood and even through puberty, there did not appear to be a tendency toward a disappearance of the existing difference in the size of the two halves of the body. In his cases, as the body grew and developed, the difference noted in infancy persisted, tending neither to disappear nor to increase in extent. From what has been mentioned, it appears that disproportions in the size of symmetrical parts of the body tend to equalize themselves in time in certain persons, whereas in other persons they persist during the entire span of life. To date, not any treatment has been suggested which is of value in ameliorating the condition, except the building up of the shoe for the shorter lower extremity so as to give relief in locomotion.

The acquired form of true hypertrophy is less common than the congenital type. The case reported by Simpson [12] in a girl who, at the age of 8 years, had developed a unilateral hypertrophy of the true type of the left lower extremity may be an example of the acquired type. The skin of this extremity was warmer than that of the right leg and presented extensive varices which were absent on the right side. The author believed that in this case the greater blood supply of the left leg resulted in an overgrowth of all the tissues vascularized, including the bones.

The false hypertrophies (see classification) constitute those enlargements of portions of the body involving only the soft tissues without the contiguous bones being affected. The false hypertrophies may be divided into certain different types, of which Milroy's disease is first considered. In 1892, Milroy [13] reported twenty-two cases of congenital or hereditary edema in six generations of a family comprising ninety-seven persons. The disease presents certain characteristics which are listed as follows:

1. The disease is a congenital condition, often being familial.
2. The edema is not due to any apparent cause, either general or local.
3. The edema is limited to one or both lower extremities and usually grows steadily with corresponding normal growth of the body until puberty.
4. The edema is permanent and yields to pitting.
5. The swollen limb is painless, and constitutional symptoms do not occur.

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12. Simpson, B. S.: A Case of Unilateral Hypertrophy, Edinburgh M. J. **33**:623 (Oct.) 1926.

13. Milroy, F. W.: An Undescribed Variety of Hereditary Edema, New York M. J. **56**:505 (Nov. 5) 1892.

Although Milroy laid stress on the fact that the edema is present at birth, Meige,[14] who, in 1898, reported eight cases resembling Milroy's disease in four generations, found that it developed later at a constant period after birth (puberty). Hope and French,[15] who, in 1908, reported thirteen cases in forty-two persons during five generations, observed that the edema developed after birth at a variable period (infancy, childhood or not until after puberty). The latter authors described a certain constitutional reaction, which often periodically complicated the condition present in the lower extremities. One or more acute attacks of fever and vomiting were associated with pain in the swollen extremity or extremities. These acute attacks lasted from three to four days, and during this time, the edema increased. Hamman,[16] Greig [17] and Painter and Bean [18] have also described conditions in their patients similar to Milroy's disease, and from the reported cases it appears that the disease does not show a characteristic involvement of the skin. The skin is firm and tense, and pits with prolonged pressure. However, some subcutaneous fibrosis is present together with the edema in the soft tissues. The bones are never involved, so that usually lengthening of the affected limbs does not occur.

The etiology of Milroy's disease (congenital or hereditary edema) is not known. Hope and French and others state that the edema in these cases is secondary, not to gross structural changes in the blood vessels or lymphatic passages, but to an error in the functions of these vessels, presumably or at least possibly resulting from erroneous functions in the nerves supplying them. On the whole, these authors think that the acute attacks complicating the condition are not due to sepsis but rather to vasomotor troubles.

Once established, the disease is permanent, and a direct effect on longevity does not occur. The disease has a good prognosis, except for the inconvenience that the enlargement of the extremity or extremities produces. With regard to treatment, Rolleston [19] suggested rest in bed and local heat for reducing the swelling. Hope and French tried the application of a bandage in their cases. They found that continuous use of a bandage decreased the swelling sufficiently to allow the patient to experience little discomfort from the swollen parts. The

14. Meige, H.: Dystrophie oedemateuse hereditaire, Presse méd. **102**:341, 1898.

15. Hope, W. B., and French, H.: Persistent Hereditary Edema of the Legs, Quart. J. Med. **1**:312 (April) 1908.

16. Hamman, L.: Milroy's Disease, M. Clin. N. Amer. **1**:182, 1917.

17. Greig, D. M.: Congenital Edema or Milroy's Edema, Edinburgh M. J. **22**:230 (April) 1919.

18. Painter, C. F., and Bean, H. C.: Hereditary Edema (Milroy's Disease), Boston M. & S. J. **184**:479 (May 12) 1921.

19. Rolleston, H. D.: Persistent Hereditary Edema of Lower Limbs, Lancet **2**:805, 1902.

latter method of relief does not lead to a cure, for even after many years of continuous use of a bandage, its removal for a certain length of time results in a return of the swelling. The following case of congenital edema will illustrate this form of treatment:

A well nourished white boy, aged 10 years, was seen first on April 2, 1927. At that time he had an enlargement of the left lower extremity, first noticed at the age of 7 months. An examination showed that the circumference of the left leg was 39 cm. at a level 10 cm. below the patella, while the right leg was 26 cm. in circumference at the same level There was no definite increase in length. The skin of the swollen extremity was smooth and firm. With prolonged pressure, pitting was obtained, especially over the lower half of the limb. Biopsy revealed some fibrosis in the subcutaneous tissue. The roentgenograms did not show any definite involvement of the bone. The Wassermann, Pirquet and Mantoux tests gave negative reactions.

On July 30, 1927, the boy was ordered to bed for a few days, and then an elastic roller bandage was applied from the knee to the dorsum of the foot; the parents were instructed to compel the boy to keep the bandage on when he was up and about, and to remove it only at night when he was in bed. The patient was seen ten days later, and then the left leg was found to be 30 cm. in circumference, 10 cm. below the patella. The thigh had not enlarged, but the dorsum of the foot had increased in size to a slight extent.

On Dec. 3, 1927, the patient was again seen and then the leg was 29 cm. in circumference. Two small openings in the skin, one on the medial side of the arch of the foot, and the other above the ankle anteriorly, had developed. From these openings, a yellow fluid resembling thin jelly drained, wetting the shoe and stocking. Six days later the drainage was less, and the leg had meanwhile decreased in size so that at the level of 10 cm. below the patella it was 27 cm. in circumference.

The progress was favorable until Jan. 14, 1928. Then the patient began to take the bandage off during the day. He would take it off while he was in school, replacing it sometimes when he returned home. The bandage, therefore, was applied only a short time each day, and, as a result, at the next examination the left lower extremity had increased in size so that it measured 34 cm. in circumference, 10 cm. below the patella. The importance of keeping the bandage applied continuously during the entire day was emphasized, and the parents promised to cooperate as much as possible.

Congenital elephantiasis is an interesting condition which often proves difficult to differentiate from congenital edema. In 1898, Jopson [20] described two cases of the former occurring in patients aged 1½ and 4 years, respectively. In these children a marked, firm swelling of both lower extremities, extending from the feet as high as the knees, was present. The increase in size was due to a thickening or an infiltration of the skin and the subcutaneous tissues. There were thick pads over the dorsal surfaces of the feet, and the bones did not appear

20. Jopson, J. H.: Two Cases of Congenital Elephantiasis, Arch. Pediat. **15**:173 (March) 1898.

to be involved. Elterich and Yount [21] reported two cases of congenital elephantiasis occurring in a girl, aged 6 weeks, and in a boy, aged 6 years. A Kondoleon operation on the latter patient yielded a piece of tissue which on microscopic study revealed an extensive fibrosis replacing the subcutaneous-adipose tissue. Ruh and Dembo [22] reported a case seen in an infant girl, who presented a swelling of the left leg, thigh and foot, the left labium majus, the right shoulder region and the right arm, hand and fingers. In addition, complete macroglossia

Appearance of patient with Milroy's disease at the beginning of the roller bandage treatment.

and edema of the right lower lip, the right ear and the right upper and lower eyelids were present. The authors considered a congenital change in the lymphatic system as the cause of the condition present in the child, and therefore call it "congenital lymphangiectatic edema"

21. Elterich, T., and Yount, C. C.: Congenital Elephantiasis, Am. J. Dis. Child. **29**:59 (Jan.) 1925.

22. Ruh, H. O., and Dembo, L. H.: Congenital Lymphangiectatic Edema, J. A. M. A. **84**:1410 (May 9) 1925.

instead of "congenital elephantiasis." The latter term has been applied to conditions in which there is either a fibrosis or an increase of the adipose tissue in the connective tissue layers (the corium and the tela subcutanea) of the skin associated with a variable distention of the lymph and the blood passages observed at or soon after birth and considered due to trophic or inflammatory disturbances dating probably from the fetal period of intra-uterine life.

Congenital hemihypertrophy of the false type may present a condition that appears similar to Milroy's disease or congenital elephantiasis. In infancy and childhood either congenital edema or congenital elephantiasis involving one lower extremity may easily be confused with congenital hemihypertrophy of the false type in which the lower extremity reveals the greatest amount of enlargement. Five of Lenstrup's eight patients had hemihypertrophy of the false type. In this condition there is a variable hypertrophy of the soft tissues together with an enlargement of the muscles, but involvement of the bones does not occur. Roentgenograms never reveal any skeletal changes.

Elephantiasis may be classified as an acquired form of false hypertrophy (see classification). It is a pathologic condition in which a thickening of the entire skin (the epidermis and the corium) and the subcutaneous tissue occurs. This change is preceded by and associated with lymphatic and venous stasis, which in turn is due to any obstruction of the lymphatic and venous passages. The mechanical interference brings about only a regional or localized edema without outstanding histologic changes in the tissues. The latter condition is brought about by a low grade infection in the area in which the lymph and blood flow has been disturbed. There is a change in the appearance of the skin, for elastic fibers disappear in the corium, and the underlying subcutaneous tissue reveals hypertrophic and hyperplastic changes associated with distended lymph and blood spaces. In advanced forms, the skin is pigmented and covered with papillomatous growths and fissures, while the muscles may undergo a fatty degeneration.

SUMMARY

1. A classification of the hypertrophies of infancy and childhood is presented with the hope that it will be of some value in the diagnosis and possibly in the prognosis and the treatment of these conditions.

2. The true hypertrophies involve the skeletal system as well as the other tissues. The skin may present areas of pigmentation, nevi and telangiectases over the hypertrophied portions of the body. Pitting of the skin is not a characteristic feature.

3. The false hypertrophies do not involve the skeletal system. In Milroy's disease the skin undergoes little change and some fibrosis

occurs in the subcutaneous tissue, while in congenital elephantiasis more changes occur in the skin and subcutaneous tissue, with involvement of the lymphatic and venous passages. Pitting of the skin is obtained easily with prolonged pressure in Milroy's disease.

4. The true hypertrophies and the false hypertrophies (especially Milroy's disease and congenital elephantiasis) may closely resemble each other during infancy and early childhood and therefore are of special interest to the pediatrician.

Pediatric Biographies

SEBASTIAN OESTEREICHER
?—1550

JOHN RUHRÄH, M.D.
BALTIMORE

Oestereicher, the all but forgotten physician of Ruffach, Alsace, who afterward practiced at Colmar, has his name linked with pediatrics in view of the fact that he used Roelans' text as the basis for a work which was popular in the sixteenth century. Not a great deal is known about him, but he is frequently mentioned in the archives of the period and apparently was a personage. His first book, printed in 1538, dealt with the work of Paul of Aegina. From this worthy, he turned his attention to Roelans, whose treatise is not easy to read. He rewrote the text, changing it considerably and adding material of his own. As he himself states, he translated it out of the "kitchen Latin." Sudhoff says that Oestereicher made a readable book of Roelans' text. The first edition was printed by Westheimer in Basle in 1540. In this edition, he mentions Roelans' "A quodam Cornelio nomine, Archiatro Mechlingense dedicatum." From the fact that it was reprinted several times, it was evidently popular. One beautiful edition was the work of Gulielmus Rovillus in Lyons, in 1549. To this was added some Hippocratic aphorisms dealing with the diseases of children.

Roelans was to have still another commentator in the person of Nicolaus Fonteyn (Fontanus), who reprinted the text of 1540 together with the "Aphorisms," but alas, by this time Roelans was forgotten and his name does not appear, only that of Oestereicher.

The nineteen aphorisms are of considerable interest. The following translation of them is by Dr. Albert Alleman, of the Army Medical Library.

1. A wet-nurse of good morals, good constitution and in the prime of life is always to be chosen.

2. If nurses keep a good diet, they will produce milk of good composition, supplying rich juices to the growing child.

3. Up to dentition, feed the child on milk alone.

4. Since we are made of it and nourished by it, the mother's milk, generated from accustomed and known blood, is more suitable to the infant's welfare than other natural milks.

5. As young goats fed by sheep produce finer hair, and lambs fed by goat's milk produce coarser wool, so too, children brought up by strange mothers differ markedly, in essential characteristics, from their own mothers.

6. Those who abandon their infants, who thrust them from themselves and give them to others to bring up, cut and destroy the spiritual bond and the affection by which nature binds parents to their children.

7. You can tell that an infant has been sent away from home to nurse by its eyes: for the strong affection for the mother is slowly and gradually extinguished and is centered alone upon her who nurses the child, which has no further inclination or love for the one who gave it birth.

8. Moderate crying of the child before feeding tends to dilate the respiratory organs, strengthens the others and to cleanse the head.

9. Teething begins in children at the seventh month, but those who absorb milk more readily develop teeth earlier.

10. Since it is not well to add fuel to fire, a well-brought up child should seldom taste wine and its nurse not at all, for it heats the body and fills the head with vapors, sometimes producing rage and insanity.

11. Lest its growth be impeded, a child should not be troubled with too much or too violent exercise from seven to fourteen years. During that period the spirit should be adorned with good manners and suitable knowledge.

12. Good mental habits are corrupted by bad habits in relation to food, drink and exercise, by what is seen and heard and by bad music.

13. Children who have been ailing for years, through bad mental habits, are cured by giving an opposite direction to the workings of the mind.

14. Inordinate mental emotion in small children should be strenuously prevented, wherefore the nurse should be prudent and expert as to the child's habits.

15. When the body is growing, increasing in size and acquiring strength, it requires heat: on the other hand, when it begins to decay, to hasten rapidly to ruin as something matured and decayed, it is of necessity immoderately cold.

16. Wine and beer are harmful to children because they befog the brain and perturb the mind by heat.

17. There are three ways of lightening the pangs of infancy; to give it the breast, gentle handling and a pleasant modulation of the voice.

18. When the infants' bowels are clogged with dry feces, they may be loosened by a few drops of turpentine or an ounce of honey.

19. Red coral suspended around the suckling's neck, from the mouth to the stomach, prevents the vomiting of milk and aids in digestion.

News and Comment

AMERICAN PUBLIC HEALTH ASSOCIATION TO MEET IN CHICAGO

The Fifty-Seventh Annual Meeting of the American Public Health Association will be held in Chicago, October 15-19, with headquarters at the Hotel Stevens. The American Child Health Association and the American Social Hygiene Association will meet with this organization.

DEATH OF PROFESSOR DI CRISTINA

The distinguished Italian pediatrician, Professor Giovanni di Cristina, director of the pediatric clinic at the University of Palermo, died, Feb. 27, 1928, at 52 years of age. He was known for many different contributions to medical literature on many subjects, especially those related to contagious diseases.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

Normal and Pathologic Physiology of the Stomach. E. Lesne and M. Coffin, Rev. franç. de pediat. **3**:613, 1927.

This study concerns gastric motility and the chemistry of the gastric secretion. Although the roentgen ray was used in studying the motility, the authors feel that one is better able to determine the amount of stasis by aspiration of the stomach contents after varying intervals. Stasis is considered pathognomonic of pyloric stenosis. The study of the chemistry showed marked differences from the adult, little free acid being found at any time and none while milk was present. The secretion varied according to the type of milk ingested. The athreptic infant showed a normal total acidity only in the presence of human breast milk or ass's milk.

Leslie, Evanston.

The Determination of Blood Sugar in Children by the Method of Weiss and Reist. Luigi Cartagenova, Riv. di. clin. pediat. **25**:733, 1927.

Only 0.1 cc. of blood is required in the Weiss-Reist method for determining blood sugar.

In each of thirteen patients (in whom thirty-five examinations of the blood were made) with diphtheria, the blood sugar was found to be 102 (from 0.048 to 0.083 per cent), whereas in six patients (fourteen examinations) with non-diphtheritic tonsillitis and laryngitis, it was regularly higher (from 0.088 to 0.110 per cent).

Action of Various Extracts on Body Growth. M. Raspi, Riv. di. clin. pediat. **25**:750, 1927.

In this preliminary paper, the author reports the results of some experiments in which tadpoles, new-born rats and infants were fed extracts from various tissues of cattle. When extract from thymus was given, a distinct increase in growth was noticed in every case.

Higgins, Boston.

Effect of Bessau's 10 per Cent Concentrated Rice Water on Gastric and Duodenal Secretion. Kurfarew and Patuschinsky, Arch. f. Kinderh. **82**:87 (Sept. 3) 1927.

The absence of the gallbladder reflex justifies the opinion that the fluid secreted is a mixture of pancreatic and intestinal juice. The reaction of the duodenal contents changes in the direction of increasing alkalinity, from p_H 6.5 to 7.2. The juice secreted after the introduction of rice water possesses good digestive qualities as regards trypsin and, especially, diastase. The diastase content is considerably greater than that of natural juice of the period immediately preceding secretion. The rice infusion evokes a considerable increase of secretion during the first succeeding work period, but does not, in any way, disturb the further behavior of the gland as to its regular alternation of rest function.

Rice water (10 per cent) is only a weak stimulant of the function of gastric gland. It stimulates duodenal secretion and evokes an abundant secretion of a mixture of duodenal juices. Therefore, the use of rice water is indicated in cases in which the stomach is in a resting condition and the burden of digestion is transferred to the duodenum, with the resulting need for its alkalinity to be raised. It is to be recommended for all children who have a tendency to fermentative processes.

Sanford, Chicago.

METABOLISTIC PECULIARITIES OF THE GROWING ORGANISM. P. GYORGY, T. BREHME and M. B. BRAHDY, Jahrb. f. Kinderh. **118**:178, 1927.

In the past year, Warburg and his co-workers have directed attention to the great significance of sugar fermentations occurring in the absence of oxygen. In studying the growth of the embryo of the sea urchin, he found that it could continue in an atmosphere of pure nitrogen, producing enough lactic acid from grape sugar to keep it viable and able to produce dividing offshoots after several days. He then found that the embryos of more highly organized *Metazoa* fermented grape sugar into lactic acid, but with this difference, that the fermentation occurred in an atmosphere of nitrogen but not of oxygen. In other words, under completely aerobic conditions, the cell lives entirely by the process of respiration (or oxygen consumption and carbon dioxide production), and fermentation is absent. The reaction is a pure oxidation, but under anaerobic conditions its metabolism is a fermentation.

The mode of production of this lactic acid in the embryos is explained by Warburg on the basis of the observations of Meyerhof with reference to the physiology of muscle. Meyerhof shows that there is a reversible reaction between carbohydrate and lactic acid in the presence of oxygen. If this occurs in relation to embryonal cells, then when respiration is diminished by high fermentation, aerobic lactic acid should appear, whereas by the increased respiration of the growing cell enough respiratory exchange occurs completely to depress fermentation. Respiration and fermentation are therefore interdependent, and Warburg has applied the term "Pasteur reaction" to that interdependence.

Fermentation is completely inhibited by oxidation only under ideal conditions in vitro. The respiration of an embryo in Ringer's solution is interfered with sufficiently for aerobic fermentation to occur. Likewise, if the embryo is placed in an atmosphere of nitrogen for several hours and then again under optimal aerobic conditions, respiration is permanently depressed and aerobic lactic acid appears. If Ringer's solution is replaced by serum, the aerobic fermentation of the embryo disappears.

One observes, therefore, that the growing cell possesses a tendency toward aerobic glycolysis, no matter how sensitive its respiration is nor how easily a small injury to respiration prevents enough oxygen utilization to hinder the complete disappearance of lactic acid. The younger the cell, the easier it is to produce an aerobic glycolysis. Warburg found that even in adult cells a small aerobic glycolysis could be produced.

The authors observe, therefore, that the rapidly growing organism is the most, and the adult organism the least, fermentative, or, as Warburg says, "No growth wthout fermentation."

Yet, these results have all been arrived at after experiments with material in vitro, and with cells and tissues; so the question arises whether these theoretical conclusions may be applied to other growing organisms, i. e., in children, in whom one would expect, especially in infants, evidence of rapid glycolysis. The only way to measure glycolysis in children would be by measuring the end-product—lactic acid—in the blood or urine and by comparing it with that of the adult. This is complicated by the fact that Warburg found that embryos already do not possess any more aerobic glycolysis and that in the organism, the aerobic and anaerobic conditions are mixed.

Another method, then, would be to disturb the Pasteur reaction by some anticatalytic process, as may be done with copper sulphate ester, etc. The question is further complicated by the fact that glycolysis in the blood depends on the p_H, the bicarbonate content, the rate of oxygen consumption, changes in blood sugar, the effect of the internal secretions, the body temperature and muscular activity. It is possible only to miminize the inevitable errors by making a large number of investigations of lactic acid under as nearly the same conditions as possible.

The method for determining lactic acid was a modification of the micromethod, for serum phosphorus, the Bell-Doisy-Briggs method, for serum calcium, the Kramer-Tisdall method.

Between March and July, 1926, and November, 1926, and May, 1927, 786 determinations of lactic acid were made in infants. It was found that in the older infants, the average lactic acid content was 10.2 mg. per hundred cubic centimeters as compared to 13.8 mg. per hundred cubic centimeters in young infants, or a difference of 35 per cent. Warburg's statement "No growth without glycolysis" seems to apply also to experiments in vivo, and it also seems that the oxidative processes in vivo are not sufficient to inhibit glycolysis completely. The average value in the first trimester of life was found to be 18.7 mg. per hundred cubic centimeters, or 83 per cent more than in grown infants. The significance of lactic acid for growth is not known. It was also found that there were seasonal variations in lactic acid content paralleling the seasonal variations in growth shown to occur by Weinberger. This has also been shown to be true of the phosphate curve.

Evidence is pressed that lactic acid produced in the intestine is destroyed in the liver and does not reach the general circulation and that the lactic acid content is not of exogenous origin.

It is shown that in rickets the average values are 12.3 or 12 per cent below the normal. Others have shown that blood sugar is less actively catabolized in rachitic persons. In tetany, lactic acid is greatly increased.

In a group of anemic infants, the average lactic acid content was 21.1 mg. per hundred cubic centimeters. Because of diminished respiration, the glycolysis in anemia in line with Warburg's observations, evidently is increased, for it is found that as the anemia disappears, the lactic acid content falls.

THE FATE AND SIGNIFICANCE OF THE DONOR'S ERYTHROCYTES IN THE BODY OF THE RECIPIENT. J. W. MOLDAWSKY, Jarhb. f. Kinderh. **118**:215, 1927.

In order to determine what significance the injection of blood has for the recipient, Moldawsky determined to investigate, by supravital staining of blood for reticulocytes, their reaction following transfusion. It can be definitely stated that the immature erythrocytes (the reticulated red cells) are up to this time the most reliable index of the activity of bone marrow, since they rise or fall parallel with erythrogenetic activity. The author finds that after transfusion, there is a lowering of the reticulocyte count, from which it is concluded that transfusion allays erythrogenetic activity. The change for the better in the blood picture at the same time indicates that the transfused cells continue to live a definite time, replacing the missing erythrocytes, and after this period of rest, the bone marrow reacts with renewed energy.

It is desirable, after transfusions, to follow the patient up with reticulocyte counts in order to determine the effect of transfusion and the opportune time for giving additional transfusions.

TRAUTMAN, Milwaukee.

Nutrition

RECENT LITERATURE REGARDING ERGOSTEROL AND THE ANTIRACHITIC VITAMIN D. EDITORIAL, J. Chemotherapy. **146**:4 (Jan.) 1928.

A short but concise review of the recent literature on ergosterol in the treatment of rachitis and spasmophilia is presented. Daily doses of irradiated ergosterol in amounts of from 1 to 4 mg. will bring the blood chemical determination rapidly to normal in from ten to thirty days. Roentgenologic control shows a zone of preparatory calcification even after the tenth day of treatment, and in all cases an undoubted growth of new bone was observed.

INFANTILE SCURVY ASSOCIATED WITH DRIED MILK: REPORT OF A CASE. PAUL LETONDAL, Union méd. du Canada, January, 1928.

The author reports a case of infantile scurvy in a child, aged 12 months, who was fed exclusively on dried milk. This milk was prepared by the hot

drum process. Under these conditions the diagnosis was made from a painful pseudoparaplegia and hemorrhages of the gums. The roentgenograms were characteristic.

SANFORD, Chicago.

AZOTEMIA AND ATHREPSIA. P. NOBECOURT, Rev. franç. de pediat. **3**:601, 1927.

Nobecourt objects to the explanation of his position in regard to azotemia and athrepsia given by Rohmer et al. (*Rev. franç. de Pediat.* **3**:277, 1927), namely: that at the base of certain digestive troubles there is a primary lesion of the kidney having as a consequence an increase of the urea of the blood; that this azotemia finds two clinical expressions — the somnolent form and the athreptic form — and that azotemia is thus a cause of athrepsia. He reviews the frequency with which he has found azotemia associated with athrepsia, and although it may be dependent in some cases on a functional disturbance of the kidney, he feels that it is for the most part an evidence of tissue autolysis, and not a cause of the athrepsia.

AZOTEMIA AND ATHREPSIA (RESPONSE TO M. NOBECOURT). P. ROHMER, Rev. franç. de Pediat. **3**:611, 1927.

Rohmer does not find azotemia existing with athrepsia to the same extent as Nobecourt did. He admits that it may be an index of the gravity of the condition, but considers it only an accessory symptom.

LESLIE, Evanston.

USE OF ACIDIFED MILK AS A PERMANENT DIET. R. O. LUNZ, Arch. f. Kinderh. **82**:145 (Sept. 3) 1927.

Acidifed milk mixtures were fed for a period of five months to a series of forty-five children varying in age from 2 weeks to 2 months at the beginning of the observation period. The lactic acid milk was prepared by the method of Marriot. Twenty-one of the children were given citric acid milk for a period of approximately two months. The citric acid milk was made by adding 4 Gm. of pure citric acid to 1 liter of milk. At the end of four weeks the infant was being fed entirely on this mixture, with an addition of 5 per cent sugar.

The majority of the children, even in the first months of life, digested the acidifed milk in suitable dilutions well, and throve much better on it than on the ordinary sweet milk formulas.

SANFORD, Chicago.

THE PATHOGENESIS OF DIGESTIVE DISTURBANCES IN INFANTS: X. THE BLOOD ACID-BASE EQUILIBRIUM IN ACUTE FEBRILE INFECTIONS. E. SCHIFF; W. BAYER and S. KARELITZ, Jahrb. f. Kinderh. **118**:17, 1927.

After reviewing the literature, the authors propound the thesis that in fevers an alkalosis is produced, except, of course, in the fever of inanition and in those fevers in which carbohydrate is primarily withheld. Attention is also directed to the fact that in severe digestive disturbances an acidosis occurs in spite of an eventual rise in temperature.

In these experiments the authors determined the hydrogen ion concentration of blood serum electrometrically and the acid and basic ions (the basic ions being Na^{+}, K^{+}, Ca^{++}, Mg^{++}, the acid HCO^{-}_{3}, Cl^{-}, $HPO^{=}_{4}$) and the protein content.

In healthy infants it was found that the content of base is 180 cc., tenth normal acid and 12 per cent of the basic radicals were combined with HCO_3 and 60 per cent with chlorine (as chloride Cl^{-}); that the acid radicals found were not sufficient to cover the alkaline, for which reason there must be new radicals which were not detected by the methods used. The hydrogen ion concentration of such blood lies between 7.33 and 7.35 at 38 C.

In children of school age, the total base of the serum was 166 cc., tenth normal acid, about 20 cc. lower than in healthy infants.

In infants suffering from acute febrile infections, the total base was in most cases between 150 and 170, tenth normal acid. Its acid radicals are the same as in the healthy infant; the protein is somewhat increased, and the hydrogen ion concentration value within normal limits. The alkali reserve is normal or slightly raised.

In the symptom-complex of toxemia (one case), there was a strong uncompensated acidosis. In another child, acidosis was present. In both cases the chlorine of the blood had been greatly reduced by vomiting.

In two cases of pylorospasm, the chlorine was diminished and the alkali reserve greatly increased. The hydrogen ion concentration of the blood was definitely to the acid side. In other words, there was an uncompensated acidosis. The total base of the serum lay between 187 and 190 cc., tenth normal acid.

The experiments have shown that in acute febrile infections the total base of the blood is lowered. This together with the facts that the acid radicals are diminished and the excretion of urinary acid increased (Hattinger), while the alkali reserve and the hydrogen ion concentration are normal or tend to the acid side, would speak for the production of an alkalosis.

The great change in hydrogen ion concentration and plasma carbon dioxide observed by Gyorgy, Kappes and Kruse was not found, but possibly there is a reason to explain this.

The normal, or slightly increased, alkali reserve of the blood seen in acute febrile infections of infants was also observed by Straub in adult pneumonias.

The experiments are not complete enough to give a picture of the acid-base equilibrium in acute infections, but with the observations of others speak for the production of an alkalosis.

CLINICAL EXPERIENCE WITH LACTIC AND LEMON JUICE MILKS. R. KOCHMANN and M. STEINBACH, Jahrb. f. Kinderh. **118**:36, 1927.

Lactic Acid Milk.—Acute Digestive Disturbances with Vomiting: In thirty-eight infants, aged from 2 to 36 months, the usual treatment began with a gastric lavage, then a six to eight hour fast, and the giving of whole lactic acid milk, in some cases with gradually increasing additions of sugar (up to 6 per cent of beet sugar). The stools quickly became normal (in from two to eight days), and gain in weight began about the second day and was progressive. Rickets, when present, was not aggravated nor cured with the diet, though light therapy and cod liver oil were used.

Acute Infectious Digestive Disturbances: In sixteen infants, aged from 2 to 12 months, in spite of anorexia, whole lactic acid milk was taken. The stools quickly became normal. All but one infant gained weight satisfactorily. A small group of sucklings and infants with acute enteric infections were treated satisfactorily with whole lactic acid milk.

Acute Nutritional Disturbances with Toxic Symptoms: In eight infants with dehydration, albuminuria and slow deep respirations, in only two in the second year of life was it possible to bring about recovery by whole lactic acid milk by a fast period of ten hours, then whole lactic acid milk with gradual increase in sugar up to 6 per cent. The milk was given in small amounts at small intervals at first with physiologic sodium chloride solution ad libitum. In the younger children whole lactic acid milk did not produce improvement, but only in one was it necessary to change to mother's milk entirely. In these cases whole lactic acid milk is an advance in treatment because the gain in weight begins earlier than it did when protein or buttermilk was used.

Kochmann and Steinbach have found that casein in vitro is digested much better by pepsin when lactic acid is added than when hydrochloric acid is added to produce an equal hydrogen ion concentration.

Chronic Digestive Disturbances: Of 50 infants, aged from 2 to 12 months, six sucklings in the first four months of life with frank decomposition could not be nourished with whole lactic acid milk alone. One became worse. One did not improve, even with mother's milk. In the others, whole lactic acid milk and mother's milk or mother's milk alone produced improvement. It appears that at these ages, when chronic indigestion is present, the use of whole lactic acid milk is contraindicated.

In older infants of this type, however, whole lactic acid milk was more effective, though in most it did not produce sufficient gain in weight. Consequently, feeding of whole lactic acid milk with mother's milk was tried. Equal parts of mother's milk and whole lactic acid milk was the first diet; when this was gradually replaced by mother's milk, the best results were produced. The subjects were those who had infections of long standing, those of a syphilitic constitution or those who had suffered from prolonged malnutrition or who had not developed normally because of some constitutional illness. In these cases, this diet was given over a period of from one to six months. At six months, vegetables and broth were added and the diet gradually increased. All improved though static growth lagged necessarily.

The authors consider butter flour and whole lactic acid milk on a par as additions to the mother's milk in this type of diet.

Lemon Juice Milk.—To sterilized milk, 2.5 per cent of lemon juice was added. Curds were not formed even on incubation at 60 C. This milk is not as easily preserved as whole lactic acid milk. On standing, it produces thick curds in a few hours; therefore, it must be refrigerated, and 6 per cent sugar added. It is taken with relish.

When given to infants with parenteral infections alone, it was not sufficiently nourishing, but it was nourishing when given with mother's milk during the first three months. Thereafter, the results were equally as good as with whole lactic acid milk.

Whole lactic acid milk is indicated in all forms of intercurrent infections of infants, especially the infectious enteritides. Only in the first two months is it to be combined with mother's milk. In chronic nutritional disturbances, whole lactic acid milk should be used only with mother's milk and is contraindicated when the condition occurs in young infants.

Lemon juice milk is indicated in all acute intercurrent infections, but especially in parenteral dyspepsia.

The value of these preparations is due to:

1. Their acidity, which produces a rapid emptying of the stomach, is antiseptic and improves peristalsis.

2. The fact that they produce a finely divided curd which is more rapidly digested.

3. By virtue of their high caloric value (1,000 calories per liter), they are antidyspeptic, quickly digested and absorbed.

To date, they are the best, though not perfect, dietaries for the treatment of infants with digestive disturbances, though in Germany they have not yet had the following that they have in America.

STUDIES IN THE PATHOLOGY OF THE ACUTE INFANTILE TOXEMIAS: III. PATHOLOGIC-ANATOMIC OBSERVATIONS IN EXPERIMENTAL INTOXICATIONS AND DESICCATIONS. EUGEN KRAMAR and ANDREAS KOVACS, Jahrb. f. Kinderh. **118**:94, 1927.

In a previous article, it was stated that the richer a diet is in albumin the greater does the organism's water requirement become. It was possible for the authors, by giving an albumin-free diet, to produce an experimental exsiccation. This made it possible for them to study comparatively experimental and clinical exsiccation, and to attempt to determine what symptoms follow on

water deficit, and which on disturbance in protein metabolism. In this paper, only the pathologic manifestations in these studies are reported.

Outspoken and pathognomonic symptoms are seen only in the liver, which is large and fatty. In infantile toxemias, the fatty liver is an expression of damage to the liver. The authors found a large fatty liver in dogs suffering from intoxication as well as in those suffering from exsiccation, grossly and microscopically indistinguishable. They believe this fatty liver to be the direct consequence of exsiccation.

Nerve changes were less constant symptoms; usually hyperemia and probable fatty degenerations occurred. These changes were also found equally in both groups of dogs.

In dogs fed a fluid-free and in others fed an albumin-free diet, like changes in the intestines consisting of localized hyperemias, petechiae and collections of lymphocytes were found. It follows that these were produced by water deficiency. In the intoxications of infants like pictures are often seen, which would therefore undoubtedly be the result of dehydration.

The pathologic-anatomic changes following experimental intoxications in dogs are: fatty liver, fatty infiltration of nerves, when intestinal symptoms are present, hyperemic areas in the intestinal mucosa, which microscopically show hyperemia and small diapedetic collections of blood.

In pure exsiccation the picture is the same, and one must therefore conclude that dehydration is its cause.

TRAUTMAN, Milwaukee.

DECREASE OF RESISTANCE AS A RESULT OF DEFICIENCY OF VITAMIN D. W. EICHHOLZ and KREITMARK, München. med. Wchnschr. **75**:79, 1922.

The specific action of vitamin D appears to be to regulate the deposits of calcium and phosphorus in predestined parts of the body. The question arises whether the adult needs vitamin D or whether he can get along without it.

It has been established that in addition to their specific actions, vitamins A, B and C also play a part so far as their lack decreases the resistance against exogenous and endogenous harmful agents. Normal resistance is not confined to the specific vitamins. In avitaminosis the resisting forces are decreased, especially as far as natural immunity and resistance to infection are concerned (dysergia).

From experiments on rats and mice, the authors conclude that lack of vitamin D in the adult lowers natural immunity.

SCHORER, Kansas City, Mo.

THE INFLUENCE OF PARENTERAL INFECTIONS AND INTOXICATION ON THE METABOLISM OF CHLORINE, CALCIUM AND MAGNESIUM. NILS MALNBERG, Acta Paediat. **6**:265, 1927.

Experiments in metabolism were carried out on children suffering from respiratory conditions, on subjects with vaccinia and those with fever as a result of typhoid vaccination. The author's conclusions are as follows:

1. Fever causes an increased output of chlorine in the urine. This occurs simultaneously with the onset of the fever or just precedes it. It is followed by a retention of chloride after which the normal balance is reestablished.

2. Either at the height of the fever or following it, there is an increased excretion of calcium and magnesium in the feces.

A perusal of the data presented, however, is not altogether convincing. The results are so irregular and the number of cases so small, that it seems doubtful if any conclusions can be drawn from them. The most consistent symptom, one which occurred in five of six cases, was a postfebrile retention of chlorine.

HOLT, Baltimore.

Direct and Indirect Light Therapy of Rickets. The Rachitic Anemia. E. Wieland, Schweiz. med. Wchnschr. **57**:169, 1927.

The author reports cases in which the symptoms of florid rickets disappeared in a remarkably short time following either direct irradiation of the child's body or the use of irradiated milk in the diet. The accompanying anemia was, however, not affected, unless or until a diet rich in iron was given. The author concludes that the two conditions are essentially independent and urges the necessity of supplying all the dietary needs of the child along with the treatment with ultraviolet rays. It is important not to give too much milk. One half liter of irradiated milk a day was sufficient to cure rickets in the older infants.

The Alleged Scorbutigenic Effect of Irradiated Milk. E. Wieland, Schweiz. med. Wchnschr. **57**:625, 1927.

In answer to Reyher's contention that irradiating milk destroys its antiscorbutic properties, the author points out that as the work was done on guinea-pigs, known to be peculiarly susceptible to scurvy, it is not applicable to human beings. Further, even in guinea-pigs, irradiation has less effect in destroying the antiscorbutic properties than has pasteurization or sterilization. It parallels the effect produced by slight cooking, and has not shown any harmful results during the two years it has been used in the clinic. In any case, the quantity of vitamin C in milk is not of great significance, since the quantity in a liter of cow's milk does not exceed that in a coffeespoonful of orange juice. The author does not claim that their results with good Swiss milk and careful irradiation would hold under other conditions. Leslie, Evanston.

Prenatal Conditions

Transmission of Protein Hypersensitiveness from Mother to Offspring. B. Ratner, H. C. Jackson and H. L. Gruehl, J. Immunol. **15**:249 (Nov.) 1927.

This article has been divided into five separate papers, which are all published in a single issue of the journal. The first deals with the "Critique of Placental Permeability." The placenta is permeable to antitoxins, precipitins, bacteriolysins, heterologous proteins, protein sensitizing antibodies, etc., in man, guinea-pigs and rabbits. The placenta is not permeable to these substances in cows, goats and sheep. A histologic difference in the placenta in the various species is offered to explain this difference in permeability. In man and *Rodentia* there is a single cell membrane separating the maternal from fetal circulation, and in ruminants there are three cell layers separating these circulations.

The second article deals with the "Rôle of Colostrum." Colostrum is an essential medium for the transmission of immunity from a mother ruminant to her new-born in goats and cattle. Colostrum plays a negligible rôle in the transmission of immunity from mother to her offspring in guinea-pigs and rabbits. Colostrum plays a negligible rôle in the transmission of immunity from mother to her offspring in the human species.

The third article deals with the "Rôle of Milk." Evidence was not found of a transmission of sensitizing proteins from the milk of nursing guinea-pigs to the suckling offspring. A critical review of the literature discloses that milk plays a negligible rôle in the transfer of antibodies to the suckling, with the exception of the mouse and ruminants.

The fourth article considers the "Passive Sensitization in Utero." It was found that horse serum hypersensitiveness can be passively transmitted to the guinea-pig in utero. This passive state of hypersensitiveness in the offspring of sensitized mothers occurred with a high degree of regularity in the authors' experiments. This passive state definitely persists for about two and a half

months and may occasionally persist, to a moderate degree, up to four months. It is also transmitted to successive litters presumably throughout the period of fecundity of the guinea-pig. This hypersensitiveness is transferred from a mother guinea-pig to her offspring through the placenta and is not hereditary in nature.

The last article deals with the "Active Sensitization in Utero." It was found that new-born guinea-pigs can be actively sensitized to horse serum, and that the passage of antigen from a mother guinea-pig to her fetus can result, in certain instances, in a definite active sensitization of the new-born, having received its sensitizing dose in utero. The close mother-fetus relationship between the guinea-pig and the human being makes it possible for the authors to offer this evidence in support of the hypothesis that infants manifesting an allergic state on first contact with a foreign protein have been sensitized in the uterus of the mother and are thus prepared for this manifestation after birth.

CHILD LIFE INVESTIGATIONS. THE CAUSE OF FOETAL DEATH IN 144 CASES. A. C. PALMER, Medical Research Council, London, 1928.

One hundred and forty-four cases were investigated. In 39 of these, the fetus was macerated. In 99 the fetus was stillborn, but was not macerated. In 6 the fetus breathed for a few seconds or a few days.

Of the macerated fetuses 14, or 35.9 per cent, were proved to be syphilitic. Of the remaining 25, in 11, fetal death can be ascribed to toxemia of pregnancy, and in 12 cases the cause of death was obscure.

In 91 of the 99 stillborn nonmacerated fetuses, the necropsy showed that the fetus had suffered asphyxia. In 55 cases, evidence of asphyxia was alone found. In all, in 73 cases, or 73 per cent, asphyxia was the cause of death.

Of the 6 infants who breathed after delivery, in 4 there was evidence of asphyxia at necropsy. In 2 there was no evidence of asphyxia, but intracranial hemorrhages showed that one of the causes of asphyxia had been present, namely, excessive pressure on the head.

Taking all the cases of nonmacerated fetuses together, in 105 cases death was primarily due to maternal disease in 27, to fetal malformation or disease in 5, and to labor in 73.

SANFORD, Chicago.

THE FATE AND DEVELOPMENT OF PREMATURE INFANTS UP TO EARLY SCHOOL AGE. MARIA COMBERG, Ztschr. f. Kinderh. **43**:462 (May) 1927.

A study of the fate of 212 premature infants on the average 53 for each of four years and 27 pair of twins, all weighing less than 2,500 Gm. at birth, is reported. Some premature infants, naturally the more the smaller the weight at birth, do not complete their first year because of their immaturity. The mortality in this series corresponds to that given by other workers for the individual weight groups. When living children were looked up after they had reached the ages of from 3 to 7 years and were, for the most part, examined except a small fraction of them who were not reached, they compared well as to development with full-term, young children, a type which up to this time has been better investigated. It appears that in premature children at early school age and somewhat before, the stimulation to growth causes an increase in length above the average, but the increase in weight does not run parallel. This condition is especially well marked in such children born of sick mothers (constitutional inferiority?) just as in children under par because of sickness, for an even longer time. Premature infants who have reached the ages of from 3 to 7 years have thin bodies, and because of faulty musculature and poor tonicity of the supporting structures they have many deformities. Postrachitic signs in these young children are seldom found, in comparison with the prevalence of rickets in premature infants. The rickets, general anemia and hernias of young premature infants are no longer seen at the ages of from 3 to 7, while megacephalus and exophthalmos, with their

possible influence on vision, are often found. These children are disposed to the exudative diathesis of Czerny. They have good resistance, if one may believe their past history, to severe illnesses of infectious origin.

Neuropathic irritability, which, like cerebral hemorrhage, appears to be a sign of special immaturity, is found frequently in children at the ages of from 3 to 7 who were born prematurely and who showed cerebral symptoms at an early age. Any connection between cerebral symptoms in the first weeks and later impairment of intelligence is not observed in these children, whose mentality is of the highest type in almost every particular. The age at which they learn to walk and to speak indicates more a lack of tone and a delayed development rather than a manifest and lasting mental injury. The activity of any particular constitutional factor, for the origin of prematurity, and any influence of inherited injury from acute or chronic disease of the mother on later development cannot be established. The prematurity itself remains as the chief cause for the peculiar development of the children. In agreement with the latest researches on the circulation in premature infants, the immaturity of the tissues, on the one hand, and the disturbance of colloidal equilibrium arising therefrom, on the other, are explained as the cause of the peculiarity of the premature constitution at an early age and its restitution with growing maturity. The constitution of the premature infant is looked on as related to the adult types of constitution, and the premature development is peculiar but does not lead to an inferior constitution. Physical and mental injuries which remain throughout life as a result of prematurity are not observed.

EMERSON, Boston.

CONGENITAL CYSTS OF THE LUNG ASSOCIATED WITH BRONCHIECTASIS. CORNELIA DE LANGE, Acta Paediat. **6**:352, 1927.

The patient reported survived two months in all. Attacks of cyanosis commenced during the first week of life and became more frequent. The physical signs were marked inspiratory collapse of the chest, hyperresonance over the left side of the chest, and dulness and increasing displacement of the heart to the right side. Terminal pneumonia developed shortly before death.

At autopsy the left lung was found to be enormously enlarged, reaching over into the right side of the chest and compressing the right lung. Considerable interstitial emphysema was found throughout the left lung. In the lower lobe of the left lung were found many large cystic cavities which connected with bronchi.

The author reviewed the literature on anomalies of this nature, and classified them into groups. The prognosis in most if not all of these cases is distinctly unfavorable.

HOLT, Baltimore.

Diseases of the New-Born

INTRACRANIAL HEMORRHAGE OF NEW-BORN. REPORT OF SIXTEEN CASES WITH THREE AUTOPSIES. ARCHIBALD D. SMITH, M. Clin. N. Amer. **11**:869 (Jan.) 1928.

Smith divides his cases into: early cases in which the symptoms came on at birth or within a few hours; late cases in which the symptoms appeared from the second to the sixth day, and mild cases. The outstanding symptoms in early cases were cyanosis, twitchings or tremors, convulsions, irregular respiration, vomiting and refusal of the breast. All of the infants except one had bloody spinal fluid with slight to moderate increase in pressure. The symptoms in late cases were: refusal of the breast, vomiting, twitchings of various muscles but no real convulsions and a faint or feeble cry. Mild cases may present any of these symptoms, singly or in groups.

The cases coming to autopsy may be summarized as follows:

CASE 6.—The birth was normal. The infant was cyanotic and moribund from the start. The bleeding time was more than twenty-eight minutes. The clotting time was twenty-eight minutes. The infant vomited and moaned continuously. The extremities and body were relaxed. The anterior fontanel was full but not tense. At autopsy, the brain showed only slight congestion and edema.

CASE 7.—Delivery was normal. Cyanosis was present. The child had general convulsions with greater movement of the left arm and leg. The fontanel was depressed. The left hemisphere was found covered with a blood clot, particularly on the posterior portion.

CASE 9.—The infant was delivered by breech extraction. The condition was poor from birth. Repeated general convulsions occurred. The fontanel was bulging. The bleeding time was fifteen minutes; the clotting time, nine minutes. Hemorrhage had occurred over both lateral surfaces of the brain and into the ventricles.

Treatment consists in the control of hemorrhage, best accomplished by direct transfusion, relief of pressure by lumbar puncture and the prevention of dehydration.

SMITH, Ogden, Utah.

INTRA-UTERINE ASPHYXIA AND INTRACRANIAL HEMORRHAGE. E. POECK, Monatschr. f. Geburtsh. u. Gynäk. **77**:442 (Dec.) 1927.

The author believes that many intracranial hemorrhages are the result of asphyxia of the fetus due to some circulatory disturbance. The circulatory disturbance may be primarily in the umbilical vessels or in the placenta. This in turn causes a circulatory disturbance and asphyxia in the fetus, which increases the action of the heart. The increased blood flow is too great for the delicate cerebral vessels and they rupture. The hemorrhage, by increasing the intracranial pressure, aggravates the asphyxia and a vicious cycle results. The threatening asphyxia is indicated by changes in the heart sounds, the passage of meconium or, if the head is visible, by the pallor of the scalp. If a hemorrhage does not occur before the circulatory disturbance is relieved, the intra-uterine asphyxia does not have serious sequelae. Several illustrative cases are cited.

BRAHDY, New York.

Acute Infections

EXPERIENCES WITH SCARLET FEVER ANTITOXIN. H. KLIMA, München. med. Wchnschr. **74**:55 (Jan. 14) 1927.

The author reports the results in a patient with scarlet fever treated with scarlet fever serum which is prepared according to the methods of Dochez and Dick. He regards the treatment with serum as beneficial.

PARAMORBILLOUS ENCEPHALITIS AND ITS RESULTS. F. LUST, München. med. Wchnschr. **74**:96 (Jan. 21) 1927.

Four cases of encephalitis in children between the ages of 2 and 8 years occurred within a period of two months. Severe cerebral symptoms were noted. In one child the symptoms were those of an encephalitis particularly of the cortex and the pyramidal system. In another there was participation of the anterior horns in the spinal cord. In two there was an encephalitis of the midbrain, that is, the lethargic form. Only one of the four patients was completely cured. In two some paralysis remained: in one, a peroneal paralysis and in the other, a cerebral hemiplegia. In the fourth case, there was a picture much like the real Gelineau narcolepsy which had to be looked on as a symptomatic postencephalitis narcolepsy.

COMPARATIVE RESULTS WITH ANIMAL ANTIMEASLES SERUM AND WITH BLOOD OF ADULTS CONVALESCING FROM MEASLES. H. ZOEPFFEL, München. med. Wchnschr. **74**:150 (Jan. 28) 1927.

The author states that protective serum against measles obtained from animals has not been effective when administered during the incubation period.

AMBERG, Rochester, Minn.

ACCIDENTAL TRANSMISSION OF VACCINIA. FRANZ HAMBURGER, Wien. klin. Wchnschr. **40**:1575 (Dec. 15) 1927.

Hamburger describes the case of a recently vaccinated school girl, who transmitted cowpox to her unvaccinated family, consisting of the mother and four children. The lesions were situated mainly on the eyelids. The author points out the fact that such accidents may be avoided by vaccinating all children in infancy, or by including every unprotected member of the family when vaccination is performed. Under such circumstances, children who have not been vaccinated for several years should be revaccinated. Hamburger states that one should take particular care to avoid vaccination in families in which there is a young child with eczema, on account of the danger of producing severe vaccinia in the latter.

CONVALESCENT SERUM IN PREVENTION OF MEASLES. J. ZIKOWSKY, Wien. klin. Wchnschr. **41**:19 (Jan. 5) 1928.

During an epidemic of measles in the contagious wards of the Franz Josef-Spital, the author investigated the Degkwitz method of preventing this disease by injecting into those coming in contact with patients with measles convalescent measles serum (M.R.S.). The serum used was obtained from adults or large children on the sixth day of convalescence. The State Sero-Therapeutic Institute tested the pooled serum from individual convalescents to prove that it was sterile, negative to the Wassermann reaction and free from tubercle bacilli as revealed by inoculation in guinea-pigs. Degkwitz has designated 2.5 cc. of this serum as a "protective unit."

When a child displayed the rash of measles, Zikowsky administered to each contact one unit of M.R.S. When contacts had been exposed to a patient with a rash of from twenty-four to forty-eight hours' duration, the protective dose was two units; when the contacts had been exposed to a patient whose rash was more than seventy-two hours old, the dose was three units. Of eighty-five susceptible children who had been exposed to measles and then treated prophylactically by M.R.S., only three (3.5 per cent) contracted measles. In these the disease was mild. The usual morbidity for susceptible child contacts, according to the author, is 90 per cent. Three children, who had been successfully protected by M.R.S., were exposed to a fresh case ten days later. One of these contracted measles, which indicated that in some instances M.R.S. confers only a brief immunity. In general, Zikowsky found the serum to be most effective when used early; when employed late following exposure either it failed to protect or a mild illness ensued.

The author states that M.R.S. was used successfully in several other hospitals in Vienna during the recent epidemic of measles. The mortality at this time ranged from 6.3 to 9.1 per cent, indicating that measles is now one of the most fatal of the diseases of childhood. It is prone to lead to serious complications, e. g., pneumonia or tuberculosis. As a secondary invader, it often determines a fatal outcome in children critically ill with diphtheria, scarlet fever or whooping cough. The author concludes from his experience that measles convalescent serum is a successful and practical method of controlling the disease, particularly in hospitals and other institutions housing large numbers of children. He advocates that M.R.S. be administered free of charge under the direction of the state boards of health.

OLMSTED, Seattle.

CLINICAL, PATHOLOGIC, ANATOMIC AND BACTERIOLOGIC INVESTIGATIONS OF A MALIGNANT ENDEMIC OF MEASLES. G. LOEWE and A. VIETHEN, Ztschr. f. Kinderh. **43**:356 (May) 1927.

Among eleven mild to moderately severe endemics of measles in Freiburg in February, 1926, one was malignant. In this home in which 106 children were cared for, the standard of health had been good and an epidemic had not occurred for years. However, it must be said that the hygienic appliances for the dormitory and playrooms and wards were not modern, and there was an insufficient number of help. In this epidemic, in which measles was complicated by diphtheria and grip, twenty-seven of thirty-three patients had lung complications. Of twenty-four small children, eighteen died, in thirteen of which autopsies were performed. The fatal complication consisted in a number of the cases of a simple bronchopneumonia the origin of which was largely due to diplococci, less often to streptococci. In such cases, usually the ones of longer duration, there was a characteristic metaplasia from ciliated epithelium of the bronchi to squamous epithelium. In cases with a rapid course severe changes occurred in the bronchial and pulmonary tissue consisting of necrotic and purulent processes, sometimes resulting in extensive abscesses of the lungs. Here a mixed infection with streptococcus was prominent. Necrosis and formation of abscess due to streptococci occurred especially when diphtheria bacilli or influenza bacilli, singly or together, could be demonstrated in the exudate of the small bronchi. In one case there was sinus thrombosis with sepsis due to streptococci. The other organs, outside of the usual diphtheric changes in the throat and frequent otitis media, showed only the usual signs of acute disease: fatty degeneration of the cortex of the suprarenals, swelling of the regional lymph glands, cellular infiltration of the periportal connective tissue and a slight hyperplasia of the spleen. Acute bronchiectasis was not observed in the cases of measles here reported, and in a case of residual pneumonia following measles, there was lacking pathologic dilatation of the bronchi. The possibility of the later occurrence of bronchiectasis on the basis of severe changes in the bronchi could not be denied.

EMERSON, Boston.

CONNECTION BETWEEN THE DICK TEST AND THE STREPTOCOCCUS ANTITOXIN CONTENT OF THE BLOOD SERUM. J. PAUNZ and E. CSOMA, Orvosi hetil. **41**:1163, 1927.

The authors have studied the connection between the antitoxin contents of the blood and the Dick test in healthy children. The summary of their work is as follows:

1. Blood serum of children and also of adults with negative Dick test neutralizes the equal amount of hemolytic streptococcus toxin which has the strength of ten skin test doses.

2. Serum of children who first gave a positive Dick reaction but were made negative through active immunization with toxin, neutralizes the toxin solution in the same way.

3. Blood serum of children with positive Dick test did not neutralize the toxin solution, but neutralizes in a few instances a weaker solution containing only two skin test doses.

4. In two cases in which the Dick test remained positive after scarlet fever, the serum did not neutralize the toxin solution. The same thing is true of cases in which the active immunization was not complete.

5. These observations were made on children over 2 years of age. Newly born babies and infants seemed to show different conditions as to the connection between Dick test and antitoxin content of the serum.

6. Results of this study seem to prove that the hemolytic streptococcus is the cause of scarlet fever.

TREATMENT OF PATIENTS WITH SCARLET FEVER WITH HUMAN BLOOD SERUM. K. KALOCSAY, Orvosi hetil. **42**:1187, 1927.

Convalescent serum, if applied early in a sufficient amount, has a striking effect on all manifestations of scarlet fever. Its effects seem to be more reliable than animal serum produced with the methods of Dick or Dochez. Its use may be indicated in cases in which anaphylactic shock has to be avoided. The antitoxin content of the convalescent serum can be determined through a Dick test. Severe forms of scarlet fever treated with convalescent serum at an early stage showed about the same good results in regard to complete recovery as mild forms of scarlet fever.

ZENTAY, St. Louis.

Chronic Infections

THE TEETH IN CASES OF CONGENITAL SYPHILIS. R. V. QUINLAN, Arch. Dermat. & Syph. **16**:605 (Nov.) 1927.

Hutchinsonian teeth were found in eleven of fifty children with congenital syphilis. Roentgenograms of the unerupted incisors in fourteen cases showed hutchinsonian teeth in two.

THE AMERICAN ORIGIN OF SYPHILIS. HERBERT U. WILLIAMS, with the Collaboration of JOHN P. RICE and JOSEPH RENATO LACAYO, Arch. Dermat. & Syph. **16**:683 (Dec.) 1927.

In 1881, Montejo published a monograph on the origin of syphilis, using Spanish sources of information. In this article, translations are given for important parts of Montejo's original source material. The evidence presented points to the American origin of syphilis.

JEANS, Iowa City.

TUBERCULOUS MENINGITIS. T. COOK SMITH, Kentucky M. J. **26**:63, 1928.

Tuberculosis in infancy is not a rare disease, and any one working in a large clinic sees it constantly. Tuberculous meningitis is always secondary to tuberculosis somewhere else in the body. It is the commonest form of meningitis in infancy, and it is the commonest cause of death in infants dying of tuberculosis. Tuberculous meningitis is practically always due to infection with human bacilli, and it is imperative for the attending physician to make every effort to locate the source of contagion. The author gives an excellent description of the symptoms and signs of the disease and of the spinal fluid. Treatment is palliative.

BRUCE, Louisville, Ky.

THE PROGNOSIS OF PERITONEAL TUBERCULOSIS. P. NOBECOURT and ILITCH DRAGOLIOUB, Rev. de la tuberc. **8**:785 (Dec.) 1927.

The prognosis in peritoneal tuberculosis is not as favorable as some maintain. The mortality of 32 per cent in the author's series of twenty-five cases is probably less than the actual mortality, since several patients were lost sight of before the outcome could be determined. Of these twenty-five patients, only five could be pronounced definitely cured after several years of observation.

The prognosis differed according to the different forms of the disease, as follows:

One patient with granular peritonitis with adhesions and perforation died.

Five patients with caseous peritonitis died.

Of fourteen patients with peritoneal tuberculosis with ascites, one died and five were clinically cured after periods of from nineteen months to six years.

Two patients with omental infiltration improved.

One patient with miliary tuberculosis died.

One patient with generalized peritonitis, but without ascites or caseation, improved, but still has local symptoms.

One patient with pelvic localization improved.

The observations of Nobecourt and Dragolioub failed to confirm the assertion of some authors that rapid development of the disease favors a good prognosis.

HEREDITARY TUBERCULOSIS. STEFAN STERLING-OKUNIEWSKI, Rev. de la tuberc. **8**:839 (Dec.) 1927.

The bacteriologic researches of the French school have recently established the existence of a filtrable virus capable of transmitting tuberculosis. Its presence in the organs of infected animals, while invisible, has been proved in many instances by animal inoculation. It has also been demonstrated that this filtrable virus may pass through the placenta and infect the fetus. The anatomicopathologic changes produced by the virus, however, differ somewhat from those produced by Koch's bacillus.

Parents long exposed to the action of the toxic products of tuberculosis may transmit certain characteristics to their offspring, in more or less attenuated form. In a positive way, these may manifest themselves by increased resistance to infection and negatively, by a heightened susceptibility to the disease. That these characteristics are transmitted not only to the direct issue of the parents but to succeeding generations seems highly probable.

SMITH, Ogden, Utah.

DIFFERENTIAL DIAGNOSIS OF TUBERCULOSIS OF THE BONES AND JOINTS IN CHILDHOOD. S. SIMON, Arch. f. Kinderh. **82**:157 (Sept. 30) 1927.

The principal pathologic condition to be distinguished from tuberculosis of the bones and joints in an infant is syphilis. In the infant with generalized syphilis there are usually syphilitic manifestations in the skin or special organs, and the typical syphilitic osteochondritis of the infant is characteristic. With increasing age, as one approaches late syphilis, the diagnosis becomes more difficult. The Wassermann reaction is negative in many instances when clinical signs and roentgenograms are characteristic of syphilis. Often tuberculosis and syphilis are both present in the same bones. Syphilis has a predilection for the diaphyses, tuberculosis for the epiphyses. There is, however, a rare tuberculosis of the diaphyses, the so-called osteomyelitis tuberculosa. In tuberculosis much swelling of the diaphysis, atrophy of the bone and absence of periostitis occur. These distinguish it from syphilis, and also from osteomyelitis provoked by the usual pyogenic agents. Syphilis attacks by preference the vault of the cranium and the framework of the nose, while tuberculosis most frequently attacks the bony border of the orbit and the lower jaw. In other parts of the body both diseases are likely to attack the same sites. The roentgenographic appearance of osteomyelitis with massive new bone formation in irregular shapes and the lack of atrophy of the bones are characteristic.

In chronic polyarthritis, the deformities occur mostly in the joints and are especially typical in fingers and toes. The greater number of joints involved is characteristic. In chronic arthritis deformans, the roentgenograms show markedly changed epiphyses and moderate atrophy of disuse, which, however, is never so severe as in tuberculosis with skeletal changes of the same degree. Tuberculous foci in the femur or acetabulum which have not yet broken through to the joint cause slightly symptoms of disease, and hence may keep one from thinking of tuberculosis. In adolescent coxa vara also, the seat of the disease is in the epiphysis of the head of the femur.

There is a group of diseases marked by pain on walking and on active and passive movement of the ankle or knee joint, and also by some limitation of movement. At first these diseases, which do not have definite names, are difficult to differentiate from tuberculosis, but after a time the symptoms disappear, and it is seen that they are not due to tuberculosis.

THE DIFFERENTIAL DIAGNOSIS OF CONGENITAL SYPHILIS. E. SLAWIK, Arch. f. Kinderh. **82**:168 (Sept. 30) 1927.

In the clinical signs of syphilis, the skin symptoms are the most striking and most frequent manifestations of this infection. Any lesions on the palms of the hands and soles of the feet are characteristic of syphilis. Syphilis should be suspected in every case of protracted umbilical bleeding and of melena. The typical syphilitic papules are usually located on the forehead and near the edge of the hair. This manifestation is especially characteristic if it spreads to the labial mucosa. A syphilitic etiology should be considered in every protracted case of icterus neonatorum. It should also be considered in every case of staphylomycosis of long duration, and in every case of tuberculosis of the bone. This is especially true in early infancy when there are multiple localizations. Syphilis may exist in these conditions in combination with other causes, and if these causes are eliminated and improvement does not occur, antisyphilitic therapy should be tried.

It must be remembered that the Wassermann reaction of the blood of parents of an evidently syphilitic child may be negative; also that the negative Wassermann reaction in a young infant is not of much value. Fetal death before term should always suggest syphilis.

SANFORD, Chicago.

Internal Diseases

HOOKWORM DISEASE CAUSING THE BLOOD PICTURE OF PRIMARY HEMOLYTIC ANEMIA IN AN INFANT. WILLIAM ALLAN, Ann. Int. Med. **1**:605 (Feb.) 1928.

A case of hookworm disease in an infant, aged 12 months, with a blood picture simulating a primary hemolytic anemia, is reported by Allan. The infant recovered after blood transfusion followed by thymol therapy.

THE BLOOD PICTURE IN PURPURA. NATHAN ROSENTHAL, J. Lab. & Clin. Med. **13**:303 (Jan.) 1928.

Rosenthal presents a classification of purpura based on a clinical and hematologic study of 172 cases. The pathologic blood pictures are reported in detail. He suggests three main groups, divided as follows:

(1) Those due to diminution of blood platelets or thrombocytopenic purpura: (*a*) acute thrombocytopenic purpura, (*b*) chronic thrombocytopenic purpura and (*c*) symptomatic thromocytopenic purpura associated with other diseases. (2) Those due to changes in the function without diminution in the number of blood platelets or chronic hereditary thrombasthenic purpura (rare). (3) Those due to changes in the capillary walls, as in jaundice, hypertension with nitrogen retention, vitamin deficiencies, etc.

Rosenthal concludes that the blood picture is diagnostic only in the thrombocytopenic group.

GIBSON, Elkhart, Ind.

THE ETIOLOGY OF PERNICIOUS ANEMIA. BEAUMONT S. CORNELL, Medicine **6**:375 (Sept.) 1927.

This article may be summed up briefly in the author's conclusion:

"Pernicious anemia appears to be a superstructure of blood system and nervous changes superimposed upon an unknown but characteristically fluctuant foundation. Of this foundation we know nothing, but conceive of achlorhydria as its constant and only obvious expression. It is not impossible that several different factors may bring the unknown fluctuant process into operation. It is further possible that this process depends chiefly upon idiosyncratic characters of the patient. The wide-spread tissue involvement found, and the peculiar mass of biochemical changes suggest that this fundamental process is a disturbance of metabolism."

ROYSTER, University, Va.

ALBUMINURIA IN CHILDREN. A. ROWAND and A. MAITLAND RAMSAY, Practitioner **119**:288 (Nov.) 1927.

In a series of 172 children between the ages of 6 and 16, who were under observation for several years in the James Mackenzie Institute, 33 have shown albuminuria at some time, many recurrently and a few, persistently. This series includes three children who were convalescing from acute nephritis. The other children were not ill but were selected because of poor family history, bad surroundings, etc.

Focal infection, such as boils, tonsillitis, carious teeth and nasal catarrh, was found to accompany the albuminuria. In several of the children, the albuminuria seemed to be of the orthostatic type.

A similar group, from 2 to 6 years of age, was studied at the Child Welfare Center. Both groups showed more than twice as many girls affected as boys.

Even in the purely functional type, the authors consider that albuminuria is a symptom of impaired health and that "the kidney is suffering with the rest of the organism from some source of mischief for which it is not itself responsible."

They believe that the cause of albuminuria is due to a congestion of the glomerular capillaries with increased permeability of the walls, caused by the presence of a toxin in the blood. One (Ramsay) describes a condition in the fundus ruli which he calls the toxic or muddy fundus which frequently accompanies the albuminuria.

The condition is treated by removal of the foci of infection and improvement in general health. Limitation of the child's activities is undesirable.

GELSTON, San Francisco.

THE STUDY OF NOMA IN INFANCY. PRESTI-SEMINERIO, Arch. de méd. d. enf. **30**:719, 1927.

Noma or gangrenous stomatitis is, relatively considered, a rare disease; it attacks children of from 2 to 5 years, who have been enfeebled by some previous invasion such as measles or scarlatina, and involves the soft tissues of the cheeks. This process may later extend to the bony tissues as well.

The infectious nature of this grave disorder is recognized; various organisms have been reported but, as Fanton remarked, "the diversity of conclusions is the best proof that the actual etiological factor has not yet been found." It is generally believed that noma is due to a symbiosis and an exaltation of virulence in organisms implanted on a soil rendered fertile by antecedent disease. The disease usually appears as a dark area at the labial commissure in the center of a sharply circumscribed induration; ulceration soon occurs, and this destructive process is rapidly extended across the cheek, with the usual disagreeable odor and profound constitutional symptoms. Death follows in one or two weeks.

Various treatments have been advised such as excision, injection of antidiphtheritic serum and application of silver nitrate. The author presents four cases from his clinic in Messina. The first case reported occurred in a child, aged 4, who had been suffering for eight months with infantile leishmaniasis (kala-azar) but who unhappily had been treated for malaria instead. The usual specific treatment for kala-azar, intravenous injections of antimony and potassium tartrate, was begun coincidently with the appearance of noma; instead of spreading, as was expected, the ulceration immediately showed a tendency to diminish and on the sixth injection or twelve days following the first, the area involved had totally cicatrized.

Another case of kala-azar in a child, aged 4½ years, who likewise showed a characteristic ulcer rapidly spreading over half of the lower lip and practically liquefying the tissue, was treated with antimony, and a coincident recovery of cancrum oris was noted, although in this patient there was great loss of tissue and a deforming scar.

Subsequent to this, two patients were brought to the clinic in whom typical Leishman bodies were found after puncture of the spleen and in whom also noma was complicating the situation. The first patient died following the third injection of antimony and potassium tartrate from an unascertained cause; the ulceration in this child's cheek and mouth had been definitely arrested. In the second child, it was impracticable to exhibit specific treatment on account of a coexisting nephritis, and with only local remedies the patient died in ten days of combined uremic poisoning and septicemia.

Presti-Seminerio urges clinicians to give this remedy precedence in the management of noma.

AMESSE, Denver.

TREATMENT OF HODGKIN'S DISEASE.. L. LORTAT-JACOB and P. SCHMITE, Paris méd. **63**:452 (Dec. 3) 1927.

The authors discuss various treatments of Hodgkin's disease, namely thorium X, benzene and arsenic. They cite a unique case in which the patient was treated by serum taken from another patient with Hodgkin's disease, who had been treated with roentgenotherapy. Their method was to inject 9.5 cc. of this serum in ten days of a first series, and 11 cc. in ten days of a second series. The results were spectacular. The red cells increased from 2,800,000 to 4,300,000, while the leukocytes fell from 22,800 to 7,800. Roentgenotherapy was then given, and after twenty-four exposures the patient was apparently cured, as all the functional disturbances had ceased. The weight had increased 12 Kg.; the glandular masses had disappeared and the blood formula was normal.

HYDATID CYSTS IN THE LUNG OF THE CHILD. LUIS MORQUIO, Arch. Latino-Am. de Pediat. **21**:669, 1927.

This eminent authority calls attention to the great frequency of the condition in his pediatric services. Several rare and unusual cases are reported emphasizing the extraordinary symptomatology which may accompany this pathologic condition.

One patient, a child at the age of puberty, showed intense and periodic hemorrhages of the lung due to a small hydatid cyst. In another case, a large pulmonary hydatid cyst opened and discharged spontaneously without causing the least functional alteration. In connection with a third case, the author points out the great importance of etiologic factors and their true evaluation in differential diagnosis of this condition from other conditions of the lung accompanied by hemoptysis and roentgenologic shadows.

SCHLUTZ, Minneapolis.

DIAGNOSIS OF ASCARIASIS OF FULLEBORN'S CUTIREACTION. H. BRUNING, Arch. f. Kinderh. **82**:6 (Aug. 5) 1927.

In an antigen prepared from pig *Ascarides*, Fulleborn's cutireaction was found to be a valuable aid in the diagnosis of ascariasis. This reaction was of value in two thirds of the cases in which *Ascarides* were found, and in four fifths of the cases in which they were not found.

SANFORD, Chicago.

THE CLINICAL PICTURE OF PURPURA FULMINANS. HANS KNAUER, Jahrb. f. Kinderh. **118**:1, 1927.

A case of purpura fulminans is presented, differing only from Henoch's classic description in that hemorrhages were present in the mucous membrane, in this case from the bowel and urinary tract. The characteristics of the case were the sudden onset of a massive ecchymosis in the thighs in a previously healthy girl, with prostration, leukocytosis, secondary venous thromboses and anemia, a normal bleeding time, an enormous decrease in plasma fibrinogen (one-twentieth of the normal), a normal blood calcium, a total absence of

clotting in vitro for three days and a normal platelet count. A determinate cause was not found. Following several transfusions of citrated blood, there was a complete clinical recovery and restoration to normal of fibrinogen, cell count and clotting time, with involution of the lesions.

Attention is particularly directed to the diminution in fibrinogen and the absence of clotting in vitro. These, with the sex, normal bleeding time, normal calcium and platelet count, set the case distinctly outside the pale of scorbutus, thrombocytopenic purpura, hemophilia and infectious purpura. Unlike the total continuous absence of fibrinogen in the rare condition known as pseudohemophilia described by Opitz, in this case the diminution in fibrinogen was transient.

A reason was not discovered for the profound changes in the blood in this case.

THE MANAGEMENT OF JUVENILE DIABETES WITH SYNTHALIN. H. HIRSCH-KAUFFMANN and A. HEIMANN-TROSIEN, Jahrb. f. Kinderh. **118**:47, 1927.

The discovery that guanidine lowered blood sugar led to the development of several guanidine compounds which were more glycolytic but less toxic. Of these synthalin, the preparation of the firm of C. A. F. Kahlbaum (of as yet undivulged formula), was brought forth as the most satisfactory in its insulin-like action. Because of its slower action, it is contraindicated when an immediate insulin-like action is desired, as in precoma or coma. The prolonged action makes it possible to intermit a day from time to time in the course of synthalin treatment.

The use of synthalin in children is complicated by the fact that their margin of safety must be much smaller than in adults, and that its effect milligram per milligram on blood sugar may be more profound than in the adult, just as the effect of insulin unit per unit often is more profound in children. Only one case (Morowitz) has been reported of a hypoglycemic syndrome in the use of synthalin when used exclusively and not in combination with insulin.

The maximum dose of synthalin was considered to be 1.5 mg. per kilogram of body weight. The full hypoglycemic effect is obtained first for only eight or nine hours and sometimes for two days after treatment is begun. When it is desired to replace insulin therapy by that with synthalin, it is sometimes weeks before the dose of insulin can be appreciably reduced without a rise of blood or urine sugar.

In children under 4 years, the effective dose of synthalin is too near the toxic to make its use practicable.

The treatment is begun with small doses, usually 5 mg. twice daily, with an intermission every fourth day. The dose is circumspectly increased to produce a reduction of blood and urine sugar. The symptoms of overdosage are malaise, anorexia and then vomiting. These crises were often avoided by giving cholagogues such as sodium dehydrocholate. If, after such treatment, glycosuria does not ensue, a combined insulin-synthalin therapy may be started. One may in this way use smaller quantities of insulin.

The best results with synthalin were obtained in children in whom the diabetes was of short standing. Gain in weight and development was satisfactory, except in children under 4. It seems, to, that in intercurrent infections, when synthalin is used, the blood and urine sugar is not greatly affected.

THE ACTION AND CLINICAL SIGNIFICANCE OF PARATHYROID (EXTRACT-COLLIP). T. BREHME and P. GYORGY, Jahrb. f. Kinderh. **118**:143, 1927.

Parathryoid extract-collip produces a rise in blood calcium, a small but definite diminution in blood phosphorus and a tendency toward acidosis with unchanged alkali reserve in tetanic and nontetanic infants. This picture is the "mirror image" of the blood chemistry of infantile tetany. The hormone produces a fall in lactic acid of blood; the blood chlorides and their cations remain within normal limits.

In the urine of normal, nontetanic children the hormone produces an increase in titratable acidity, ammonia, potassium and phosphorus, as well as total nitrogen and organic acids.

In latent rachitic tetany the hormone produced a more marked excretion of ammonia, as it did in nonrachitic controls. On the other hand, the titratable acid and the excretion of phosphates were barely changed.

In a patient with puerile tetany, the urine showed several variations from those previously discovered.

The total excretion of calcium and phosphate in two cases was not changed by the giving of the hormone. Consequently, the high excretions of calcium and phosphorus in the urine are only evidence of a change in the excretory mechanism and probably are closely related to the acidotic tendency.

The action of parathyroid extract-Collip is inconstant. This, with the associated side reactions (vomiting, pallor and diarrhea), contraindicates its general clinical usefulness, though its value in experimentation is not to be minimized.

The ordinary infantile tetany is not of parathyroid origin. In one case of puerile tetany, intensive antirachitic treatment did not control it. Possibly this was a case of parathyroid tetany.

THE PATHOGENESIS OF PYURIA. HANS SCHLACK, Jahrb. f. Kinderh. **118**:224, 1927.

It is demonstrated by culture of the urine of normal infants that only 45 per cent of such urine is sterile, which indicates that more than the mere presence of bacteria is necessary to produce pyuria.

In a study of twenty-four cases it was found that there are two distinct groups of cases relative to the development of pyuria, running entirely different clinical courses. In the one group there precedes for a longer or shorter time a bacteriuria which for some reason develops into a pyuria. In premature and new-born infants whose diet consists entirely of mother's milk and whose intestinal flora is predominantly *B. coli*, the bacteriuria is predominantly that of *B. coli* and by some is considered to be of metastatic origin. The onset of this type is usually not accompanied by fever or symptoms.

The onset of the condition in the second group is with symptoms of renal disturbance or hematuria; in the author's material, the onset occurred largely in connection with infections or digestive upsets, with casts, epithelial cells and leukocytes. In most cases the causative organism was *B. coli*. In only a few cases were other organisms present at the onset, and the disease changed to a *B. coli* pyuria. The observations in the urinary sediment with dehydration (casts, epithelial cells and high specific gravity) seem to be a symptom of renal damage which is not dependent on bacteriuria.

In infants it is questionable whether the mode of infection is ascending or descending, and an analogy cannot be made between the adult and infant in this respect. In the case of an idiot, a mixture of colon bacillus was injected into the bladder. Severe pyuria was produced in eighteen hours, but in four days it had entirely subsided.

TRAUTMAN, Milwaukee.

THE VALUE AND THE MECHANISM OF EFFECT OF BLOOD TRANSFUSIONS IN PURPURA DUE TO THROMBOPENIA. KRASSO, HUGO, Wien. Arch. f. inn. Med. **14**:377, 1927.

Blood transfusions are absolutely indicated in acute, rapidly fatal cases of purpura due to thrombopenia. The effect of the transfusion is one of substitution. The blood of the donor furnishes the blood of the recipient with the missing elements, in a form suitable for physiologic function.

The transfusion of a large amount of blood is particularly successful in cases in which the noxious agent is not continually operative, thus leading to

chronic relapsing states. It can take the place of splenectomy. Although the mechanism is entirely different, the ultimate effect of both forms of therapy is the same in purpura due to thrombopenia.

INSULIN AND BLOOD PRESSURE. RUDOLF STRISOWER, Wien. Arch. f. inn. Med. **14**:429, 1927.

Blood pressure falls after injections of insulin. The author believes that the hormone of the pancreas has a central effect analogous to pituitary and the secretion of other ductless glands, such as the thyroid and hypophysis.

SCHLUTZ, Minneapolis.

STATISTICS AND PROPHYLAXIS OF HEART DISEASE. E. NOBEL, Wien. klin. Wchnschr. **41**:125 (Jan. 26) 1928.

On the basis of recent English statistics assembled by Pirquet, Nobel plotted the mortality curves of several diseases, including rheumatism in its various forms. The curves in total rheumatic disease (chorea, acute rheumatic fever, rheumatic endocarditis) closely resembled those in acute rheumatism and in appendicitis; they displayed a sharp rise and fall in the second decade, followed by a gradual decline in later years. The author thinks that the similarity of the curves of acute rheumatism and appendicitis, suggest the possibility of a hitherto unsuspected etiology for the latter disease. The curve for acute endocarditis, which was lower than those just mentioned, displayed a maximum death rate in the third decade. This, Nobel states, is explained by the fact that forms other than rheumatic endocarditis were included in this group. The maximum mortality for chronic rheumatism occurred at the ages of 70 to 75 years.

In a second graph, the author showed that the chief causes of death in infancy and childhod are bronchitis and pneumonia. From personal observations, he has found that from five and one-half to eighteen and one-half years after an attack of acute rheumatism or chorea, approximately one half of the patients display rheumatic sequelae. He thinks the prognosis more serious in heart disease following chorea than in that occurring after rheumatism. Nobel and Hecht have observed that when tonsillectomy is performed after the fifth year of life, it decreases the tendency to angina in 90 per cent of the cases; but that children operated on before that age receive benefit in only 60 per cent of the cases. The author states that hemolytic streptococci are demonstrable in the heart valves of the majority of patients with endocarditis and that in the future a method of active immunization against the cardiotropic strains may be evolved.

OLMSTED, Seattle.

MEDIASTINAL PNEUMATOCELE FOLLOWING PNEUMONIA IN AN INFANT. J. DUKEN, Ztschr. f. Kinderh. **43**:339 (May) 1927.

An infant, aged 4 months, had pneumonia six weeks before admission, which lasted a long time. Though the cough was not severe, the child remained miserable, lost its appetite, became thin, whined all the time and at entrance was hoarse and cyanotic but not feverish. In front, over the right lung and over the sternum, tympany was present, but a respiratory murmur was not heard. In the back, on the right side of the chest, dulness and almost bronchial respiration without râles were present. The roentgen ray disclosed a smooth walled, round space the size of a fist, which it seemed must correspond to a cavity. Puncture resulted in the release of air, and the signs of pressure and hoarseness disappeared. After the puncture was repeated on the sixth day, the shadow disappeared and the child recovered. The whole picture is that of an air hernia, a real pneumatocele of the mediastinum. In persons with interstitial emphysema, air wanders forward in the interlobular septums to the roots of the lung, chiefly under the pleura and thence along the great vessels and the trachea.

A Cervical-Pulmonary Pneumatocele Following an Abscess in an Infant. J. Duken, Ztschr. f. Kinderh. **43**:346 (May) 1927.

In an infant, aged 9 months, an abscess quickly developed on the side of the neck. Several days later, after the swelling had been poulticed and had became smaller, erysipelas developed over the right side of the body, which subsided and left a fluctuant right hand. The swelling in the neck then became fluctuant and on incision yielded much seropurulent exudate, and two days later, with light pressure, many air bubbles. On admission to the clinic, the infant was very sick, with short, superficial breathing and an expiratory cough resembling pertussis. Hemolytic streptococci were recovered from the incision. It was noticed that the swelling increased when the infant cried vigorously and disappeared when the infant became quiet. When the swelling was present a peculiar murmur could be heard over it, such as could be heard over a hollow space containing compressed air. The percussion note was hollow.

The roentgen ray showed an air-filled cavity with a communication leading downward, apparently to the trachea. An iodine preparation was injected into the neck in front of the fluoroscope screen and was seen to run into the cavity in the upper right lung and to stay there except when, with a little pressure, it appeared in two small bronchi. There must have been a ball-valve communication of the cavity with the bronchial tree. It is suspected that at the same time the abscess formed in the neck, another one appeared in the lung and the two came into communication. This cervical pulmonary pneumatocele was widely opened, and the child bids fair to recover.

The Urogenital Diseases in Infancy. Siegfried Levy, Ztschr. f. Kinderh. **43**:494 (May) 1927.

Communications concerning the inflammations of the kidney in infancy, especially those without demonstrable cause in the form of infection or toxic injury are scarce. With consideration limited exclusively to infancy, Levy has reviewed critically the nephritides observed from 1918 up to the present at the Infants' Hospital at Hamburg on the basis of Finkelstein's classification of constitutional impairment and characteristic inflammation of the kidneys. The mortality in these seventeen cases was high, 82½ per cent, in contrast to an average mortality of 19.4 per cent for the hospital as a whole, and, contrary to accepted opinion, was due primarily to nephritis. Grouped according to etiology, the cases were divided into group I, nephritis developing in a course of erythrodermia desquamativa; group II, in the course of congenital syphilis; group III, in the course of acute infections and of disease sui generis. Autopsy was not performed in any case. Because of the difficulty of an accurate clinical diagnosis of nephritis in infancy, the attempt to group the inflammations, according to Volhard-Fahr's scheme, could have only a limited value. Levy did not consider the mixed forms which came to light at autopsy, and grouped his cases according to the most important symptoms. A toxic injury of the kidney was ascribable as the cause of nephritis in five cases of erythrodermia desquamativa, group I, analogous to the observations of Kaumheimer in the impetiginous eczema of older children. In group II, nephritis was traceable in five cases in all probability to syphilis; three of these gave the clinical picture of nephroses, one showing waxy casts in the urine. One patient was thought to have a glomerular nephritis and another a septic interstitial focal nephritis. Two patients apparently suffered a toxic injury from treatment with mercury. In both groups the significant high mortality was noteworthy as being higher than that corresponding to the primary disease. In group III, the author found nephrosis three times and glomerular nephritis twice, and one case which did not clinically fit into Volhard-Fahr's scheme. In one case, the cause of the onset of nephritis was not found. Some characteristics of nephritis in infancy were described briefly, particularly the gray-gold color of the skin, which is referred to insidious decomposition and the activity of the disease on the psyche of the child.

In conclusion, a case was reported in which the condition appeared to be nephritis sui generis and which could be looked on etiologically as a toxic injury, perhaps, occurring during pregnancy. Since an increase of the glomerular nephritis occurred under internal treatment, a decapsulation was performed for the first time in an infant, with good results, and a prompt recovery was obtained. For this reason, such a procedure is recommended, even in infancy, in suitable cases before the occurrence of uremic symptoms.

EMERSON, Boston.

DYSPNEA IN CHILDREN. D. HERDERSCHEE, Nederl. Tijdschr. v. Geneesk. **71**: 2599, 1927.

In this article, the author (who is chief of the department for infectious diseases of the town hospital at Amsterdam) discusses the diagnostic difficulties to which dyspnea in children may give rise. The cause of the dyspnea in children nearly always lies in the respiratory tract, whereas in adults one must always think about the possibility that dyspnea is caused by general disease (coma diabeticum, cardiac asthma and uremic asthma). In the experience of the author, disease of the lower respiratory tract, especially acute pneumonia with only few local symptoms and bronchial asthma, is in children often mistaken for laryngeal stenosis. In severe forms of laryngeal stenosis which make operation necessary one nearly always has to deal with diphtheria. The author gives his experience in 458 cases in which operation was performed. In 369 of these, micro-organisms resembling diphtheria bacilli were found morphologically. In 256 of the patients with laryngeal diphtheria, the bacilli could be cultivated from both the pharynx and from the larynx. *B. diphtheriae* was found only sixty-four times in the larynx and only forty-nine times in the pharynx, though culture from the larynx was made only once.

As regards the success of the tracheotomy in relation to the age of the patient, the author's results almost corresponded to those of Bokay, who found a mortality of 49 per cent in patients under 2 years of age and a mortality of 19 per cent in those above this age.

Serum was given in all cases of laryngeal stenosis in which the diphtheritic origin was seriously suspected. The severe forms of serum disease of long standing were often seen, especially in those patients whose blood picture even before the injection showed a large percentage of lymphocytes. Serum disease was seen in 85 per cent of the patients treated for the first time with serum and in 88 per cent of the other cases. As regards the type of the serum exanthem, since the use of a serum from which the proteins that do not contain the antitoxin are removed, the erythema iris is rarely to be seen. Recurrences and reinfection with diphtheria and laryngeal diphtheria were not rarely seen by the author.

In laryngeal stenosis, diphtheria must be differentiated from other diseases. The author mentions as such spasm of the laryngeal muscles and swelling of the larynx, caused by irritation or obstruction through a "corpus alienum" or a tremor, infectious processes of the larynx or its surroundings, or by abnormal irritability of the nervous system. The differential diagnosis with catarrhal croup must be made most frequently. The laryngitis in measles may give severe difficulties which are not solved if Koplik's spots are found. Acute retropharyngeal abscesses may give diagnostic difficulties, especially in young children. In some cases a dyspnea that necessitates tracheotomy appears at the same moment that the serum disease does.

At the end of his article, the author discusses some examples of laryngeal stenosis in which the cause is situated outside the larynx, i. e., enlarged thymus or tumor in the mediastinum.

S. VAN CREVELD, Amsterdam.

MYXEDEMA FRUSTE (HYPOTHYROIDISM) IN CHILDREN. EMIL WIELAND, Schweiz. naturforsch. Gesellsch. **2**:264, 1927.

Attention is called to a mild type of hypothyroidism occurring in children, characterized by (1) disturbances of growth; (2) changes in the skin (a water rich, pasty skin, seldom containing fat and dry or with greatly diminished perspiration); (3) a sluggish, passive disposition and (4) habitual obstipation. Doubtful cases may be checked by the roentgen ray, but the author questions the usefulness of basal metabolic tests.

LESLIE, Evanston.

Nervous Diseases

THE NERVOUS COMPLICATIONS OF VARIOLA, VACCINIA AND VARICELLA, WITH REPORT OF CASES. R. E. WILSON and F. R. FORD, Bull. Johns Hopkins Hosp. **40**:337 (June) 1927.

Twelve cases are reported in which varicella was followed by encephalomyelitis and myelitis, which developed between four and fifteen days after the onset of the disease. Recovery was practically complete in all cases.

R. C. JAMIESON, Detroit.

ALLERGY AND EPILEPSY: ANALYSIS OF ONE HUNDRED CASES. RALPH H. SPANGLER, J. Lab. & Clin. Med. **13**:41 (Oct.) 1927.

Spangler says that recent investigations point to the probability that the immediate cause of the convulsion, in so-called idiopathic epilepsy, arises from a disturbance of metabolism. Certain clinical, hereditary, immunologic and therapeutic evidence is presented which points to allergy as an etiologic factor in some cases of epilepsy. He tabulates and analyzes the clinical observations in 100 consecutive cases of epilepsy in adults (43 women and 57 men) with especial reference to allergic manifestations in the ancestors and in the patients. Children were not included in the summary since he considers it necessary, prior to the age of puberty, to exclude spasmophilia and so-called "reflex convulsions" before a definite diagnosis of epilepsy can be established. Among the summarized deductions from his tables and data are the following:

1. Gastro-intestinal hypersensitivity to cow's milk or other substitute for mother's milk appears to be a decided factor in the development of infantile convulsions in the atopic child. In this series of 100 cases of epilepsy in adults, 62 patients were breast fed, 8, or 12.9 per cent, of whom had convulsions in infancy. Of the 38 patients who were bottle fed, 24, or 63.1 per cent, developed convulsions in infancy.

2. Bottle feeding (protein sensitivity to milk or food foreign to the mother) may be a more potent factor in the development of infantile convulsions than difficult or instrumental birth. Twenty-five of the 100 patients were first-born infants; 16 of these were breast fed, 5, or 31.2 per cent, of whom had convulsions in infancy. Of the 9 first-born children who were bottle fed, 4, or 44.4 per cent, had infant spasms. Twenty of 100 were instrumentally delivered and 10 of these were breast fed, among whom 3, or 30 per cent, had convulsions in infancy. Of the 10 instrumentally born who were bottle fed, 8, or 80 per cent, developed infant convulsions.

3. Clinical evidences of allergy in epilepsy often show themselves early in infancy. When food is substituted for mother's milk there appear at times, especially in the child with an allergic ancestral history, periodic vomiting, cyclic diarrhea and other digestive disturbances, which may be accompanied by hives, eczema or other sensitization symptoms. Spangler points out that it

is under these conditions that infantile convulsions are apt to appear. He says that so-called "reflex spasms" in infants, especially those attributed to teething, are frequently found on close analysis to be evidence of protein hypersensitivity which occurs coincidently with the change in the form of diet the child ingests when teething. In this series of 100 adult cases of epilepsy there was a history of digestive disturbances with convulsions during infancy in 32 of the patients. Twenty-four, or 75 per cent, of these were bottle fed and 8, or 25 per cent, were breast fed. Moreover, among epileptic patients he frequently sees other allergic clinical manifestations. In 54 of the 100 patients in this series the following other allergic conditions occurred; migraine, 19; hives, 18; eczema, 11; asthma, 3, and hay-fever, 3.

4. Food history, i. e., tabulation of all articles of food ingested, for the purpose of determining and eliminating the sensitizing agent, has been of more clinical value in allergic epilepsy, in Spangler's hands, than food skin tests, which have proved disappointing. Four illustrative case histories are given. Spangler says from the cases in which he has used the ketogenic or high fat content diet he believes that its value is due more to the accidental elimination of the agent to which an epileptic patient is sensitized than to the production of acidosis or ketone bodies in the system.

5. Hereditary deductions from these 100 consecutive adult patients with recurring convulsions reveal that in 88 per cent there was a history of allergy in the immediate ancestors (parents, grandparents, uncles and aunts). The total number of ancestors showing allergic manifestations, not including convulsions, was 158, as follows: 44 of the ancestors had asthma, 12 hay-fever, 17 urticaria, 8 eczema and 77 migraine. Of these, 110 were on the maternal and 48 on the paternal side. In 12 of the 100 patients who gave no ancestral allergic history, there were 5 whose ancestors had convulsions. The total number of ancestors having convulsions was 24, but in 8 of these the convulsions did not persist after childhood.

6. Certain immunologic evidence is given that points to the anaphylactic nature in some cases of epilepsy. The possibility of the transference of epileptic sensitization in the human by the transfusion of blood from an epileptic to a nonepileptic with resulting convulsions, as reported by Boston and Henry, and the convulsions occurring in animals following the injection of blood from humans suffering with epilepsy as reported by Cuneo, are cited.

7. Therapeutic evidence of allergy in epilepsy is indicated by Hajos' observations that experimental and clinical anaphylactic sensitiveness are decreased by epinephrine and by extract of the parathyroids and the posterior lobe of the pituitary, since all of these agents have been found of aid in the treatment of various cases of epilepsy. Spangler says in his experience epinephrine has been of especial value in treating series of convulsions and in status epilepticus, but that its daily use has not proved of much benefit as a preventive measure in petit mal or grand mal seizures.

8. When the allergen or causative agent cannot be determined, or, if known, cannot be removed in epileptic patients who have an hereditary or personal history of allergy, and in whom a leukocytosis occurs after a convulsion, nonspecific desensitization by venom protein solution, when regulated by the percentage of eosinophil cells in the differential blood count, has proved of value in decreasing the patients' state of allergy.

HUNTER, Philadelphia.

BRACHIAL PLEXUS OBSTETRICAL PARALYSES AND REPORT OF A CASE. VINCENT GILIBERTI, J. Nerv. & Ment. Dis. **66**:449 (Nov.) 1927.

Giliberti states that this type of injury, the second largest of the birth palsy groups, may occur in normal confinement in rare instances when a

combination of contracted pelvis, a large binacromial diameter and prolonged labor exist, but is produced most frequently in those cases requiring artificial aid, and in head presentations more often than those of breech, shoulder or foot. Abduction, elevation and backward movement of the arm while the head is bent toward the opposite side is the manipulation that is most apt to produce injury to the brachial plexus. Pressure on the plexus by traction with a finger or hook in the axilla and traction exerted on the shoulder to accelerate the delivery of a head are also sources of danger. The nerve fibers and bundles are usually torn and ripped apart; the break may occur at any point from the spinal origin of the roots to the lower part of the plexus. When rupture of the nerves has occurred, the ends retract and scar formation prevents regeneration. The distal portion degenerates in its entirety, the central portion only at the severed end with neuroma formation. The changes of the spinal cord are slight, but are most marked in cases of avulsion of the root.

The upper arm type of paralysis, due to injury of the fifth and sixth cervical roots, is most common and involves the deltoid, brachialis anticus, biceps and supinator longus. The lower arm type of paralysis, lesions involving the seventh and eighth cervical and the first thoracic roots, affect the triceps, the flexors of the wrist, pronators, flexors and extensors of the fingers and small muscles of the hand. When the lesion is close to the vertebral foramens of the eighth cervical and first thoracic a Horner's syndrome is also produced. The combined type of paralysis is due to a lesion of the entire plexus or most of it and is probably most often caused by dislocation of the shoulder with pressure on the plexus.

Electrical reactions assist in determination of prognosis; if electrical reactions are normal or but slightly altered ten or fifteen days after the onset, complete recovery should occur within six weeks; if partial reaction of degeneration is found, recovery should be complete in three or four months; a complete reaction of degeneration means a guarded prognosis as complete recovery will not occur in all cases. The author thinks that the prevention of obstetric paralyses is, in a large measure, feasible.

Treatment in early stages consists of demobilization of the injured arm by means of a splint from hip to axilla which holds the arm elevated in abduction at an angle of 90 degrees. This causes approximation of the torn ends, and should be continued until function is restored. Massage, heat, hydrotherapy and exercises should be used during this time but in such a way as not to interfere with the postural treatment. If signs of regeneration have appeared within one year the mechanical and physical treatment should be continued, if not, neurosurgery should be resorted to. The matter of habit paralysis is considered. Contractures should be corrected by gradual and graded stretching, an adjustable splint being used for this purpose and forceful rupture of adhesions being avoided. The case presented is interesting, but mention is not made of the treatment that was instituted in this instance.

KUBITSCHEK, Philadelphia.

INFANTILE CEREBRAL PARALYSIS OF THE ATONIC-ASTATIC TYPE OF FOERSTER. JUAN ORRICO, Arch. Latino-Am. de Pediat. **21**:675, 1927.

The author describes four cases of this rare form of infantile cerebral paralysis. All of the cases were characterized by the peculiar syndrome described by Foerster: the hypotonicity of the muscles of the neck preventing raising of the head; the general flaccidity of the trunk muscles with resulting inability of any active movements; the exaggeration of the knee reflexes; the spasmodic contractions of the lower extremities when the infant is raised and made to attempt to stand.

In one of the cases the condition did not set in until the age of 22 months, and was then ushered in with acute onset such as vomiting, fever and diarrhea.

Poliomyelitis, encephalitis and the amyotrophic condition of Werdnig-Hoffman could be ruled out. It was apparently an acquired condition rather than the usual congenital type.

In all four cases there was marked mental abnormality. Two of the patients gave a positive Wassermann reaction.

EXTRAPYRAMIDAL SYNDROME: HEMICHOREA WITH LEFTSIDED ATETOSIS. JOSÉ MARÍA ESTAPÉ, Arch. Latino-Am. de Pediat. **21**:690, 1927.

The author presents a case showing an extrapyramidal syndrome characterized by athetotic choreic movements confined entirely to the left side of the body and involving the head and the upper and lower extremities.

The condition developed progressively but did not interfere with the locomotion or speech of the child. The intelligence remained entirely normal.

Anatomically and topographically, the lesion is probably a crossed lesion in the caudad nucleus and the right lenticular nucleus. Microscopically, the author suggests a perivascular sclerosis of the right deep branch of the artery of Silvius and especially of the artery supplying the right lenticular nucleus.

The chief etiologic factor in the case was apparently hereditary congenital syphilis. The disease was resistant to antisyphilitic as well as to all other forms of treatment.

SCHLUTZ, Minneapolis.

Diseases of the Ear, Nose and Throat

AN EPIDEMIOLOGIC AND STATISTICAL STUDY OF TONSILLITIS, INCLUDING RELATED THROAT CONDITIONS. Bull. 175, U. S. P. H. S., March 1, 1928.

These data were collected from various field studies made during the last ten years. It was found that the incidence of tonsillitis was higher among children of school age than before or after. This incidence is higher for females than males, and is prevalent to the age incidence of diseased tonsils found on physical examination. The prevalence was about equal in rural and in urban districts, but the removal of tonsils was more frequent in urban groups. The incidence of sore throat is twice as great among school children with defective tonsils as among those whose tonsils have been removed; also, the incidence of respiratory infections is greater among children with defective tonsils. The incidence of diphtheria, cervical adenitis, conjunctivitis, eye strain and decayed teeth all tend to be more prevalent among children with defective tonsils than among children with normal tonsils, or among those whose tonsils have been removed. Measurements of height and weight over a period of nine months for a group of school children did not show any advantage in the growth of one tonsil group over the other.

SANFORD, Chicago.

ACUTE PROLONGED ADENOIDITIS; EFFECT OF DIRECT PALPATION. RENDU, Arch. de méd. d. enf. **31**:73 (Feb.) 1928.

This paper is presented with the object of calling attention to a particular form of inflammation of the adenoids, characterized by fever of long duration, not commonly discussed in the textbooks. Since the discovery of adenoid vegetations by the Danish physician, Meyer, in 1868, innumerable articles have been published concerning these growths, in practically all of which they are discussed either from the point of view of mechanical obstruction or as a source of infection, contiguous or remote. At first of interest only to the rhinologist and the otologist, this condition is now a matter of everyday concern to the general practitioner and particularly to the pediatrician.

Foremost among the manifestations of infection in these vegetations is, of course, acute adenoiditis, whether developing independently or preceding otitis, bronchitis or some other invasion in contiguous organs. Rendu recites at

length three cases in children ranging in age from 20 months to 4½ years. These three cases were so similar clinically that they may be reviewed collectively. Each patient was suffering from acute adenoiditis with fever of a septic type which continued from twelve days in one instance to three weeks in another; there was a violent reaction on the part of the cervical glands, especially those along the carotids and at the angle of the jaw. This led one consultant to diagnose the condition as glandular fever. In the first patient seen, posterior rhinoscopy was not feasible and digital palpation was employed instead. Immediately following this examination the temperature fell abruptly and remained normal. The same striking result followed this maneuver in the other cases, the author explaining it, to his own satisfaction at least, on the assumption that such manipulation of the vegetations separated the lamellae of the adenoid body and possibly evacuated minute abscesses which, under some pressure, were responsible for the septic temperature and the glandular absorption. Rendu does not regard glandular fever (drusenfieber) as a clinical entity but considers the syndrome, as do Hutinel, Armand-Delille and many other pediatricians, as merely a complication of some rhinopharyngeal inflammation, commonly adenoiditis. He urges clinicians to ignore the old injunction that cautions one against traumatizing these tissues when they are inflamed, and to practice palpation particularly when fever approaches the septic type.

AMESSE, Denver.

Diseases of the Skin

ENDOGENOUS IRRITANTS AS FACTORS IN ECZEMA AND IN OTHER DERMATOSES. J. FREDERICK BURGESS, Arch. Dermat. & Syph. **16**:131 (Aug.) 1927.

Of 109 patients with eczema seen consecutively, mostly adults, 16.6 per cent gave positive skin tests to toxic substances produced by bacterial action on food products or to amino-acids. Only 2 per cent of noneczematous patients gave similar reactions. Relief was obtained in some of the patients with eczema by mild cathartics and *Bacillus acidophilus* in milk.

TREATMENT OF URTICARIA WITH EPHEDRINE. BEATRICE M. KESTEN, Arch. Dermat. & Syph. **16**:189 (Aug.) 1927.

Seventeen patients with chronic urticaria or with chronic urticaria and angioneurotic edema were treated with ephedrine sulphate by mouth. Relief or complete cure was obtained in the majority of cases.

RAYNAUD'S DISEASE. D. E. H. CLEVELAND, Arch. Dermat. & Syph. **16**:548 (Nov.) 1927.

The dermatoses associated with Raynaud's disease in the two cases reported were of a variety commonly recognized as being the result of toxemia, usually from some distant focus of infection. The author believes it reasonable to deduce that toxemia is the predominant factor in producing the vasomotor derangement which is the essential feature of Raynaud's disease.

BLOOD SERUM CALCIUM IN THE URTICARIAS. SIGMUND S. GREENBAUM, Arch. Dermat. & Syph. **16**:553 (Nov.) 1927.

As a result of determinations of blood calcium in sixty-three patients with urticaria and coagulation time in many of these, it is concluded that indication does not exist for attempting to increase the blood calcium in this condition.

In the discussion of this paper, it is stated that calcium salts are of value in some cases of urticaria even though they may not increase the blood calcium.

AN INTRACUTANEOUS METHOD OF TREATING ARGYRIA. ARTHUR WILLIAM STILLIANS and THEODORE KENNETH LAWLESS, Arch. Dermat. & Syph. **17**:153 (Feb.) 1928.

It was found that a mixture of 0.25 per cent potassium ferricyanide and 6 per cent sodium thiosulphate injected intradermally quickly removes the bluish discoloration of argyria. The injection must be made immediately after the drugs are mixed.

EPILATION WITH THALLIUM ACETATE IN THE TREATMENT OF RINGWORM OF THE SCALP IN CHILDREN. BOTHO F. FELDEN, Arch. Dermat. & Syph. **17**:182 (Feb.) 1928.

Thirty-six of forty-seven children with ringworm of the scalp were cured after one oral administration of thallium acetate in a dose of 8 mg. per kilogram of body weight. Epilation began about the eighteenth day and was complete in half the cases. In the remainder, epilation was completed by extraction with adhesive tape. Local treatment with iodine and sulphur was used in addition. Thallium is stated to be contraindicated in acute infections and nephritis and, because of its toxicity, should not be given in full dose to adults or to children approaching puberty.

THE USE OF THE "GRENZ" (INFRAROENTGEN) RAYS IN DERMATOLOGIC CONDITIONS. JOSEPH J. ELLER and GUSTAV BUCKY, Arch. Dermat. & Syph. **17**:221 (Feb.) 1928.

The biologic and clinical effects of rays of about 2 angstrom units were investigated. Such rays are somewhat longer than roentgen rays and are called infraroentgen or "grenz" rays. These rays produce erythema and penetrate only slightly, but penetrate more deeply than ultraviolet rays. In the dose used, epilation or other undesirable sequelae did not occur. Twenty-seven different skin diseases were treated. Favorable response or cure was observed in cases of acne, angioma, ringworm, basal cell epithelioma, eczema, lupus erythematosus, leukoplakia of the tongue and other conditions. In some of the conditions for which patients were treated, little if any response was noted.

JEANS, Iowa City.

ERYTHREDEMA IN A BOY OF FOURTEEN MONTHS. W. A. ALEXANDER, Trans. M. Chir. Soc., Edinburgh M. J. **35**:34 (Feb.) 1928.

The child shown by Alexander had been sick five months with atonic muscles, fretfulness, anorexia, red swollen hands and feet, desquamation and photophobia. The boy was making a gradual spontaneous recovery. This case developed while the infant was still being breast fed. Special treatment was not used.

NEFF, Kansas City.

PRIMARY TUBERCULOSIS OF THE SKIN. F. GOEBEL, Arch. f. Kinderh. **82**:257 (Nov. 11) 1927.

The case of a boy, aged 5 years, with primary tuberculosis of the skin, is presented. The author first saw the boy in consultation, when the symptom complained of was adenopathy. The original lesion was a small scar on the ankle, and immediately above this were some reticular red nodules. Sections removed and examined histologically showed an old tuberculous formation that was spreading rapidly.

SANFORD, Chicago.

Surgery and Orthopedics

SUPPURATIVE PERICARDITIS. EDWARD W. PETERSON, Arch. Surg. **16**:366, 1928.

Peterson reports the case histories and follow-up notes of three children with suppurative pericarditis who were treated surgically. The ages of the patients were 1 year, 3½ years and 14 years. The cause of suppurative pericarditis

was pneumonia, and cultures of the pericardial fluid gave growths of *Bacillus influenzae, Staphylococcus albus,* and pneumococcus type II, respectively.

Resections of one or more costal cartilages from the fifth to the seventh were performed under local anesthesia in the cases reported, but the author advocates the use of the incision of Pool, which is made through a curve overlying the fifth, sixth and seventh cartilages and involves resection of all three of them.

The first child died thirty-six hours after operation, but the other two recovered.

The author advises removal of the pericardial pus by suction at the time of operation rather than by irrigation and prefers ethylene if a general anesthetic is required.

GEORGE H. JACKSON.

CONGENITAL HYPERTROPHIC PYLORIC STENOSIS. W. E. LADD, Boston M. & S. J. **196**:211 (Feb. 10) 1927.

Ladd reports a series of 162 cases from the Boston Children's Hospital and thirty-five cases from private practice; 80 per cent were in males. The mortality in the cases in the hospital was eleven deaths, or 5.5 per cent; in the cases from private practice only one death occurred, that of an infant who for more than five months weighed under 5 pounds (2.3 Kg.); this was one of the earlier cases before the value of proper preoperative preparation was realized. Symptoms began commonly in the third week of life with vomiting of a projectile character, the vomitus consisting only of the milk ingested and never any bile. The tumor was palpable in most cases during the brief period of relaxation immediately after vomiting occurred. Roentgen-ray examination is usually unnecessary, and when it is made immediately before operation the retained barium seems to interfere with the retention of postoperative feedings.

Preoperative preparation is essential in overcoming the dehydration that usually is present. Blood transfusions seem particularly helpful. Ether anesthesia is preferred to local anesthesia. A catheter is introduced into the stomach as a routine procedure. The patient must be kept warm. An abdominal incision is made through the right rectus muscle, and is so placed that the lower border of the liver appears in the middle of the incision. Great care must be taken to avoid cutting through the mucous membrane at the duodenal end of the incision through the pylorus, as the muscle thins abruptly at this point. The mucous membrane must be freed sufficiently to allow it to pout through the wound above the serous level to insure adequate lumen of the pylorus. Appreciable hemorrhage rarely occurs and is best controlled by a silk stitch tied over a fragment of muscle removed from the right rectus. The abdominal incision should be carefully closed in layers to prevent postoperative evisceration. While the patient is still on the operating table, 2 or 3 ounces (7.5 or 11.2 cc.) of 5 per cent dextrose solution is given by rectum. One ounce (3.75 cc.) of boiled water is given by mouth one hour after operation; this is followed an hour later by 2 ounces of whey, and this is continued every two hours for the first twelve hours; also, hypodermoclysis and a dextrose solution is given by rectum if the infant is badly dehydrated. At the end of twelve hours, one-half ounce (1.8 cc.) each of whey and breast milk is given every two hours for the next twelve hours, after which the breast milk is gradually increased and the whey decreased a drachm at each feeding. Later the amount of breast milk and the intervals between feedings are gradually increased.

GENGENBACH, Denver.

THE PREVENTION OF EVENTRATION INJURIES IN LAPAROTOMIES IN CHILDREN. R. SIEVERS and T. SCHORNSTEIN, Beitr. z. klin. Chir. **139**:517, 1927.

A pathologic condition requiring eventration of the intestines in laparotomies is usually caused by some intestinal obstruction and its associated lesions. The fatal termination in such conditions is a huge distention of the intestine

or, in other words, "ileus." Ileus carries with it serious circulatory disturbances in the bowel that interfere with proper function; this results in accumulation of gas and an increase in fluid content with an ischemic necrosis of the intestinal mucosa, absorption of toxins and finally the escape of bacteria into the peritoneal cavity, resulting in a terminal peritonitis. With the tissues in such a damaged and friable state, any mechanical manipulation such as eventration may damage them to the point of perforation, unless such eventration is performed carefully.

For many years, surgeons have sought methods whereby one might safely open and explore the abdomen in ileus with a minimum amount of damage to the intestine. Moynihan and Kirschner have used a suction device whereby one might aspirate the intestinal contents, allowing the bowel to collapse and thus adding more room for exploration. This device was not successful, and surgeons continued to explore by allowing the entire bowel to eventrate but at the same time studying the problem. That such a method was to be condemned was shown by Perthes, who found that eventration as practiced was associated with a mortality of 56 per cent, while in operations in which eventration was not done, the mortality was 21 per cent. Perthes sought to overcome this by allowing the abdominal viscera to escape into a bag held to the laparotomy wound and suspending it from the side of the wound to prevent drying and cooling of the intestine. However, he did not take into account the untoward influence of the suspension of the bowel from traction on the mesenteric root.

To study the possibilities for relief more fully, the authors conducted animal experiments and studied the changes in the organism during eventration of the intestine. They found that if on complete eventration the intestine was allowed to hang down on one side or the other and cause traction on the mesentery, and at the same time the loops of the bowel were allowed to cool and dry, there resulted a fall in blood pressure of from 10 to 30 mm. of mercury and the respirations became shallow. Simultaneously, the bowel became cyanotic and the lymph channels engorged. They also found that by allowing the intestine to pass into a circular bag, all of the alterations soon disappeared. They also found that the administration of atropine has the same effect.

Therefore the authors conclude that in operations for ileus following eventration of the bowel there is produced reflexly a disturbance of circulation and respiration from the cooling, drying and suspenion of the exposed bowel. On the other hand, if one provides a bag which serves to increase the capacity of the peritoneal cavity and receives the eventrated intestine, such disturbances are minimal and the administration of atropine will tend to minimize these disturbances even more.

SURGICAL TREATMENT OF OSGOOD-SCHLATTER'S DISEASE. C. T. WILLICH, Beitr. z. klin. Chir. **140**:86, 1927.

Osgood-Schlatter's disease, a disturbance of ossification of the tibial tuberosity, also designated as "apophyseopathie," according to the author may be treated in one of two ways, and in his review of the literature he finds one group of investigators advocating conservative and another surgical treatment.

In his own series of sixteen patients with Osgood-Schlatter's disease, twelve were treated conservatively and four by operation. Of the group treated conservatively eight still had pain on certain movements from one half to three years after treatment, while four recovered in from one to two months. The four patients in the group treated surgically failed to respond to conservative management. All recovered in less than six weeks.

The author calls attention to three desirable factors to be gained from operating in such conditions; (1) a rapid disappearance of symptoms; (2) a permanent cure in most instances, and (3) an opportunity to study the tuberosity microscopically and macroscopically and thus furnish some etiologic

data. The study of his own material was identical with the observations reported by other investigators except that in one specimen he noticed some interesting symptoms which he attributed in part to the unusually long standing of the disease. He found in the center of the tuberosity an area of well-preserved bony lamellae, having a good nuclear stain. On the tibial side, these bony lamellae gradually fused with a layer of cartilage containing isolated islands of newly formed bone. Peripheral to the cartilage he found a dense connective tissue capsule completely surrounding the section with vascular connective tissue processes dipping in from the periphery. Round cell infiltration was not found anywhere. The author calls attention to the connective tissue capsule completely surrounding the cartilage and ossification center and preventing a fusion with the adjacent epiphysis.

In regard to treatment, the author advises a conservative program, such as immobilization, etc., and if this fails then operative removal.

THE SIGNIFICANCE OF THE ABSORPTION OF SODIUM IODIDE AND PASSAGE TEST IN SURGERY OF THE BRAIN AND SPINAL CORD WITH ESPECIAL REFERENCE TO THE CAUSE AND PREVENTION OF HYDROCEPHALUS AFTER OPERATIONS FOR SPINA BIFIDA. LEOPOLD HEIDRICH, Beitr. z. klin. Chir. **140**:345, 1927.

The author calls attention to a method developed by Dandy whereby one may determine the communicability of the various cerebrospinal fluid chambers and the absorptive faculty of the subarachnoid space. The method consists of the injection of 2 cc. of neutral phenolsulphonphthalein solution into the lateral ventricles, and if an abnormal condition is not present, one may recover traces of the solution from the cisterna in two minutes, from the lumbar canal in from three to five minutes and from the urine in from five to eight minutes, and in from five to eight hours, from 50 to 60 per cent is eliminated by way of the urine.

Owing to some severe reactions such as headache, vomiting, fever and collapse, the author, by using 2 cc. of a 10 per cent solution of sodium iodide instead, has prevented such reactions. The objection to this solution is the difficulty of determining its elimination quantitatively, and one must content oneself with a qualitative determination. Such a determination is made by extracting the cerebrospinal fluid or urine with one-third volume of chloroform, and then when the extract is treated with a few drops of sulphuric acid a rose red precipitate will form in the presence of sodium iodide. The author found that when this solution was injected into the lumbar canal, from three to five minutes were required for it to reach the cisterna, and from five to eight to reach the lateral ventricles normally. When the solution was injected into the lateral ventricles, the same time was required for it to travel to the cisterna and lumbar cord, respectively.

This method is diagnostic in various diseases of the brain and spinal cord. In conditions such as meningitis or tumor, the flow of cerebrospinal fluid from one compartment to another is hampered and the rate of aborption from the subarachnoid space will be delayed. In Kuttner's clinic the method has proved most valuable in determining the cause of an internal hydrocephalus after operations for spina bifida. Some observers attribute such a hydrocephalus in part to a diffuse serous meningitis resulting from the operation, and in part to operative trauma. Others look on it as a hypersecretion with lack of absorptive function which in part resides in the communication of the spina bifida sac and the overlying skin. The author calls attention to two factors, namely (1) that the spina bifida sac absorbs a great deal of fluid and (2) that after the removal of the sac this absorption is interfered with and, as a result, cerebrospinal fluid is secreted in excess to its rate of absorption.

To meet such a condition successfully, the author advises the use of sodium iodide before operation and again in from ten to twelve days after the operation for comparison. If the postoperative test reveals a delay in time of passage of the cerebrospinal fluid from one compartment to another, the place

of obstruction can be determined, and if there is a marked delay in its appearance in the urine, one may assume that there is some interference in the absorption of the subarachnoid space. He further advises, in case an internal hydrocephalus develops, a subcutaneous drainage of the cranial cavity or multiple perforations of the atlanto-occipital membrane.

OPERATIVE TREATMENT OF PYONEPHROSIS IN INFANTS. MARTHA HAGENBUCH, Beitr. z. klin. Chir. **140**:558, 1927.

In the treatment of pyonephrosis in infants there are always some types that are resistant to medical management, especially if congenital anomalies causing partial or complete obstruction to the outflow of urine are present. Occasionally pyonephrosis develops without any demonstrable anatomic change on careful examination of the removed specimen. Some observers regard all pyonephroses in children under 5 years as due to some congenital anomaly. The author reviews the literature on this subject and cites anomalies such as an incomplete double ureter with a marked hypertrophy of the muscularis of the ureter to partially occlude the lumen, an intra-uterine ureteritis, inflammations of the ureteropelvic junction, folds or valvelike prolapse of the mucosa and finally, as already mentioned, sometimes not any demonstrable anatomic factor.

The treatment is either drainage of the renal pelvis or removal of the involved kidney. Surgical measures are not always without complications, for there may be an involvement of the opposite side later, or a pyo-ureter of the remaining distal ureter, or a complete anuria.

OBERHELMAN, Chicago.

Miscellaneous

SCHEME FOR AN ORTHOPEDIC HOSPITAL, WITH MAJOR AND MINOR CLINICS, FOR THE SOUTH-EASTERN DISTRICT OF SCOTLAND. JOHN FRASER, Edinburgh M. J. (Trans.) **35**:5 (Jan.) 1928.

Fraser discusses the proposed scheme of establishing as a center an orthopedic hospital in Edinburgh, major clinic centers in the larger surrounding towns, and minor clinics in the periphery of the district. He bases the need for such an organization on the number of crippled children, probably more than 1,000, reported by the Scottish Board of Health. At present many children are on the waiting list of local hospitals. In addition to the operative work done at the central hospital, the cripples may be prevented from undergoing relapse by follow-up care at the surrounding clinics. The major and minor clinics would be in affiliation with the hospitals already established in the various communities. The plan contemplates taking care of all needy patients in this district of Scotland, so that every child will have a chance to be free of disablement.

THE OCCIPITAL BONE AND BONES OF THE SUPERIOR EXTREMITY IN RELATION TO "RIGHT" OR "LEFT" HANDEDNESS. L. B. WEVILL, Edinburgh M. J. **35**:12 (Jan.) 1928.

Wevill quotes the incidence of left-handed children, as found by Bardeleben, to be 6.8 per cent, and the number of left-handed children who have been changed to use the right as 26 per cent. He thinks it reasonable "to suppose that education of the child to use the right hand in preference to the left" might cause a change from the original conditions in the skeleton, if the child acquired skill in the use of the right hand.

Wevill has made numerous examinations of adult skulls and compares his observations with those reported in the Nubian Survey, quoted by Prof. Elliott Smith. From the study of the impression made on the occipital bone by the right cerebral hemisphere as well as from the measurements of the left humerus,

clavicle and radius as compared with the opposite upper extremity, Wevill states that one cannot conclude that changes in the skeleton prove whether the individual is "left" or "right" handed. It is only from the postmortem examination of persons whose "handedness" had been known that one can get reliable data on this subject.

NEFF, Kansas City.

POISONING FROM SUBNITRATE OF BISMUTH. LUIS D'OTTONE, Arch. Latino-Am. de Pediat. **21**:835, 1927.

Subnitrate of bismuth can produce grave symptoms of poisoning, as is evidenced by a case reported by the author. The symptoms of poisoning are slow and progressive and consist mainly in intense cyanosis, chilliness and cardiac collapse. Large doses of epinephrine prove valuable in combating collapse. This was given intravenously (1 cc.) and intramuscularly (0.5 cc. of a 1:1,000 solution).

SCHLUTZ, Minneapolis.

TWENTY-FIVE YEARS OF MEDICAL ACTIVITY IN THE KINDERASYL. L. F. MEYER, Gesundheit. f. d. Kindesalter **1**:494 (July) 1926.

The article deals with the experiences of Meyer gained by his work in the children's Home of Berlin. The mortality of the old home in 1900 was about 50 per cent. In the first year of the new home, Finkelstein showed a reduction of 10 per cent. He ascribed this result to the following factors: (1) Isolation, with the prohibition of cleansing of the mouth; (2) organization of a hospital along proper university hospital lines; that is, careful medical supervision, use of histories and daily curves, etc.; (3) breast feeding; one-tenth of the children were fed with breast milk; (4) a trained nursing staff; there was one nurse to eight or nine children; (5) development of a convalescent home or supervision of foster mothers during the convalescent period. Nevertheless, children who stayed a long period in the home still showed the high mortality of from 30 to 45 per cent. Finkelstein ascribed this to the common infections with colds. This serious mortality has in the meanwhile been markedly reduced. Meyer discusses the factors leading to this result; first, the recognition of the need of vitamins and second, the decrease in the dystrophic condition due to the more cautious use of fasting periods and the increase in the number of calories given the children. Through the use of natural and artificial light, rickets and spasmophilia have been prevented. The results of this work can be seen in the following statistics: The mortality of pneumonia has dropped from 75 per cent in 1921 to 35 per cent in 1925; that due to pyelitis has dropped from 43 per cent in 1923 to 8 per cent in 1924. The total mortality has decreased 50 per cent in the last three years. Schlossman's Gefährdungsziffer dropped from 39.8 per cent in 1920 to 7 per cent in 1925. It can be seen how good this result is from the fact that, according to Schlossman, the same figure for the total number of children born in Düsseldorf in 1920 was 4. Meyer does not believe in the spiritual injury to children in institutions. The psychic retardation is caused by physical retardation, not vice versa. He therefore believes that hospitalism finds its explanation in the inefficiency of the physician, the nursing and the feeding.

THE INFLUENCE OF THE SEASONS ON DISEASE IN INSTITUTIONS. NASSAU, Gesundheit. f. d. Kindesalter **1**:526 (July) 1926.

Nassau reports from the Berlin Kinderasyl that there also the winter peak has surpassed the summer peak of mortality. He found the usual phenomenon of tetany in the spring, rickets in the winter and dysentery in the late summer. In the case of measles, he finds a definite rise in the number of cases in the first half of the year every second year. The tuberculin reactions were much stronger in the spring. He finds the interesting result that the cases of common cold were about the same in number for all months of the year, but

that the length of illness resulting from such a cold varied greatly, there being a sharp and high peak in March and April. The increase in deaths which occurs at the same time is due almost entirely to pneumonias. Nassau finds the cause of this phenomenon in the conception of a transition period during which the days are getting warmer while the nights still remain cold. This makes it difficult to regulate the temperature in the wards. He does not deny that these may also be endocrine changes in the spring which may be responsible for an increased mortality.

THE STATISTICS GATHERED FROM THE INFANT WARD OF THE KINDERASYL AND ORPHAN ASYLUM OF BERLIN OF THE YEAR 1925. J. JAHR and HEDWIG ZWIEG, Gesundheit. f. d. Kindesalter **1**:542 (July) 1926.

The total mortality rate was 4.3. The peak of mortality occurred at the end of the first quarter, in contradistinction to the higher mortality of the early weeks in previous years. The authors ascribe this to the better results in feeding and to the fact that at the end of the first quarter the infant had lost its inborn immunity and succumbed to infection. In 1907, 46 per cent of the total deaths were caused by nutritional disturbances; in 1925, 19.1 per cent.

REICHLE, Cleveland.

HEMORRHAGES IN PUNCTURE OF THE SINUS. W. FALK, Monatschr. f. Kinderh. **36**:532, 1927.

In the pathologic material of six years, the author did not find sinus thrombosis occurring as the result of puncture of the sinus. In six cases, however, there were pial and subdural hemorrhages. He believes more care should be taken in the technic of these punctures.

GERSTLEY, Chicago.

HIGH MORTALITY OF CHILDREN IN LARGE FAMILIES. J. FRIEDJUNG, Wien. klin. Wchnschr. **40**:1578 (Dec. 15) 1927.

The author, who is director of a municipal clinic for pension mothers and other poor families, investigated the histories of 100 families in which the number of children was six or more. The mortality, including stillbirths, was 46.27 per cent. For the most part it varied directly with the size of the family. Bad hygiene, undernutrition, neglected illness and injuries were particularly frequent in this group. The older children were often retarded in physical and mental development because they had become slaves to their younger brothers and sisters. Friedjung pleads for more adequate visitation in these families by nurses and social workers.

OLMSTED, Seattle.

AN IRRITATION PHENOMENON IN ERYTHEMA EXSUDATIVUM MULTIFORME, NOT DESCRIBED BEFORE. A. PERUTZ, Nederl. Tijdschr. v. Geneesk. **85**:1481 (Oct. 22) 1927.

In sixteen of the nineteen cases of erythema exsudativum multiforme in which he applied the test, Perutz found that scratching the healthy skin with a needle caused the appearance of an eruption which corresponded in its stage to that of the other erythema lesions of the patient. It never, however, equaled them in intensity. It appeared after about twenty-four hours and lasted for from five to seven days. The fresher the case and the nearer the needle scratch to the exanthem, the more distinct was the reaction.

INFLUENCE OF ULTRAVIOLET AND RED RAYS ON THE SKIN. G. J. VAN DEN BOVENKAMP, Nederl. Tijdschr. v. Geneesk. **71**:1617 (Oct. 15) 1927.

Van den Bovenkamp sought to discover the cause of the antagonistic action of ultraviolet and red rays. (It is known that pigmentation and erythema caused

by ultraviolet rays disappear under irradiation with red rays — wave length 750-580 millimicrons.) Cantharides plaster, containing cantharides, euphorbin and turpentine, produces skin phenomena similar to those of the ultraviolet rays. Here also there is a period of latency. On each forearm of an experimental subject, a cantharides plaster was applied and left in place for three hours. One arm was then immediately exposed to red rays in a dark room for thirty minutes. On this arm no trace of erythema or blister formation appeared, while on the other arm the usual manifestations occurred and ran a typical course, the redness not disappearing for forty-eight hours. In a further, similar experiment, the plaster was left on for five hours, and the red rays were not applied until four hours after its removal, when intense redness was present and blisters were beginning to form. The rays were applied for forty minutes. In this case, the blister formation took its usual course, but the redness disappeared in twelve hours. Pointing out that the red rays exert their influence in the deeper-lying tissues, the author suggests that, by the hyperemia that they cause there, blood is withdrawn from the superficial tissue, so that the erythema fails to appear or, in case it has already appeared, quickly fades.

CARPENTER, Chicago.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

Regular Meeting, Dec. 20, 1927

MAURICE BLATT, M.D., *President, in the Chair*

JUVENILE TABES DORSALIS: REPORT OF THREE CASES. DR. HAROLD A. ROSENBAUM.

This paper will be published in full in a later issue.

EXCRETION OF CERTAIN VOLATILE ACIDS AS INFLUENCED BY DIETS OF BREAST MILK AND MODIFIED COW'S MILK. DR. JESSE R. GERSTLEY.

This paper will be published in full in a later issue.

DISCUSSION

DR. M. G. PETERMAN, Milwaukee: I would like to know whether the source of the cow's milk was always under control, and whether the acid content of the milk was known so that these factors were always constant. I should think this would make considerable difference in the fatty acids found in the milk that was fed.

DR. JOSEPH BRENNEMANN: We have always thought of babies with frequent stools as having acid stools, and all of the babies that were fed artificially had acid stools. I wonder what the observations would be if Dr. Gerstley kept on until one of his subjects was an incorrigibly constipated baby that would remain constipated after it was on the metabolism frame.

DR. JESSE R. GERSTLEY: Replying to Dr. Peterman, the fat in the mixtures of cow's milk was not controlled. We used the milk from our milk station. The routine procedure in our hospital is to have the milk examined for its fat content once a week by our chemical laboratory. During the last years the analyses have shown variations of only a few tenths per cent, the general average being a little over 3 per cent. While most scientific workers recognize that some of the volatile acids found in the stomach arise from splitting of the fat, the consensus of opinion is that the volatile fatty acids found in the stool arise from the fermentation of carbohydrate. All experimental work has shown that the fat content of the mixture does not play a part.

Replying to Dr. Brennemann, not a single patient showed constipation. Clinically, the babies were normal, but the bowel movements of all of them tended to be a little loose while they were on the metabolism frame. We are continuing this study, and perhaps later we shall find a baby of the type Dr. Brennemann mentions.

A STUDY OF TUBERCULOSIS IN CHILDREN. DR. A. LEVINSON.

One hundred and nineteen patients were admitted to the tuberculosis service of the pediatric department of the Cook County Hospital of Chicago within a period of thirteen months. Twenty of these were under 1 year of age, and sixty-three were between 1 and 5 years of age, making 69.7 per cent of the patients under 5 years of age. Eighty-three were negro children, eleven were Mexican and twenty-five were white children.

The majority of the patients showed some form of pulmonary involvement. Sixty-nine of the patients proved to have suffered from miliary tuberculosis, including meningitis, and thirteen from acute nonmiliary pulmonary tuber-

culosis; fifteen suffered from chronic pulmonary tuberculosis. In two cases that ran a chronic course, the condition was for some time considered as epituberculosis; the fatal termination of the case, however, disproved that contention.

The tuberculin skin tests were negative in all cases of miliary tuberculosis. In some cases a positive tuberculin reaction was given on admission, but negative reactions resulted as soon as the patients developed miliary tuberculosis.

The differential diagnosis constituted one of the most important problems in connection with the cases studied. The greatest difficulty was experienced in the diagnosis of miliary tuberculosis. One case in which the condition was diagnosed as acidosis proved, on necropsy, to be miliary tuberculosis. Another case, in which the patient had severe anemia, and a history of having eaten wall paper, was diagnosed as lead poisoning, but proved on necropsy to be miliary tuberculosis.

The most frequent diseases from which miliary tuberculosis in the premeningeal state had to be differentiated were: grippal infection, bronchopneumonia, typhoid fever and rickets. In the stage of meningitis it had to be differentiated from the various meningitides; acute anterior, poliomyelitis, encephalitis, tumor of the brain and abscess of the brain. At times we also had to differentiate tuberculous meningitis from typhoid fever, because of abdominal pain associated with the meningitis.

Acute pulmonary tuberculosis had to be differentiated from other forms of pneumonia, and from grippal infections. Chronic pulmonary tuberculosis had to be differentiated from unresolved pneumonia, chronic bronchitis, bronchiectasis and dulness due to heart disease. Tuberculous peritonitis had to be differentiated from typhoid fever, and suppurative peritonitis.

The following cases, which were first considered tuberculous, proved to be nontuberculous: one case of pneumococcus empyema, one of bronchiectasis, one of actinomycosis, one of meningococcus meningitis and one of acute anterior poliomyelitis.

DISCUSSION

DR. GERALD KROST: What tuberculin test was made as a routine? Dr. Levinson mentioned the fact that miliary tuberculosis shows a negative reaction and that Hempelmann found it positive. I do not think he stated what dose was used. As I recall, in Hempelmann's paper read before the American Medical Association he stated that in the intradermal test a larger dose has to be used in order to get a reaction in miliary tuberculosis. The Pirquet test is comparable to a 0.01 mg. intradermal test in sensitivitity, the smallest or beginning test dose.

DR. BRENNEMANN: We do not admit tuberculous patients to the Children's Memorial Hospital, and I think this might make a decided difference with reference to the Pirquet test. Nearly all of our patients with miliary tuberculosis give a positive Pirquet reaction, and most of the cases occur in children who have been healthy. Recently an intern asked me why miliary tuberculosis always occurs in the healthiest children. I wonder whether in the children at the Cook County Hospital a negative Pirquet reaction is not more frequent because those children have had extensive chronic tuberculosis, while in our patients perhaps only a gland or two breaks down and produces a hematogenous miliary tuberculosis. Dunne said years ago that early miliary tuberculosis could not be recognized with the roentgen ray, and we have been able to verify this a number of times. He said that when it can be recognized, it is no longer miliary tuberculosis but miliary tuberculous bronchopneumonia.

We have been carrying on a rather similar study at the Children's Memorial Hospital, where we get only the early and the late cases, and have had a man working on this problem exclusively for a year in an effort to correlate the clinical, the postmortem and the roentgen-ray observations. I will only say that we are getting some ammunition with which to counteract the pernicious habit that some roentgenologists have of diagnosing, or suspecting,

tuberculosis in nearly every case. I have learned more about the roentgen-ray observations in pulmonary tuberculosis since this study was instituted than I ever knew before.

DR. JULIUS H. HESS: I think Dr. Brennemann is right in saying that tuberculosis seen with the roentgen ray, and possibly also clinically, differs greatly from the material seen in different hospitals. It is interesting to note the statistics of tuberculosis in colored and in white people.

The high death rate from tuberculosis for the negro race is still more marked in the group, ages 0 to 11 years, than for the population as a whole. Rates for negroes in this group are from ten to twenty times as high as for the white children of the same age for the same period. In 1926, 41.04 per cent of the total deaths of children in Chicago under 11 years of age occurred among negroes, who composed only 3 per cent of the total population in this age group. In 1926, two thirds of the deaths from pulmonary tuberculosis occurred in the negro population, while one fourth of the cases of tuberculous meningitis for this year occurs among negroes. The death rate from tuberculosis in Chicago has dropped to fifth place in the white group, heart disease, nephritis, cancer and pneumonia being more frequent causes of death; but tuberculosis still causes the largest number of deaths in the colored race. Our material at the Cook County Hospital is made up largely of colored patients.

At a recent meeting we had a discussion concerning the etiology of erythema nodosum. An experience that I think worth relating is one that I had in Scandinavia this summer. Among the clinics which I visited was that of Walgren at Göteborg, Sweden. In his wards, I saw twelve patients with cases of erythema nodosum in which there could be little doubt that infection with the tubercle bacillus was the underlying factor. Walgren stated that a great deal of erythema nodosum is seen in Scandinavia in tuberculous children, and that while frequently seen, it is somewhat less prevalent in Germany and is rarely seen in Hungary.

Preceding the eruption, a mild degree of pyrexia is constant. This may be present for only a few days or for as long as a month before the eruption appears. More commonly it is of short duration. In all of his cases the tuberculin test reaction was positive during the fever stage. It thus seems to be at the moment when the pyrexia begins in these cases that the line of demarcation is formed between the pre-allergic and allergic stages, or the moment when allergy is speedily increasing. Consequently, the onset of erythema is a sign that the body is now sensitive to tuberculin.

While in most of the cases of erythema nodosum which I have seen a streptococcus infection was seemingly the background, we had a case in March and we have another one in our wards at the present time in which both of the children are tuberculous. Walgren also showed me several series of roentgenograms of epituberculous pulmonary lesions. This condition, while rare in children living in Chicago, is commonly seen in Sweden. During the past year, I have had occasion to follow two such cases in children, aged 3 and 4 years. Both have been making satisfactory progress, and in one case the symptoms in the lung have practically disappeared; the patient in the second case also shows improvement.

DR. GERSTLEY: How often did Dr. Levinson find tuberculous meningitis associated with miliary tuberculosis? The teaching that tuberculous meningitis is a termination of miliary tuberculosis is practically universal. During the last few years I have seen a number of patients dying of tuberculous meningitis, and postmortem examination did not show much tuberculous involvement of the rest of the body.

DR. BLATT: Sooner or later one finds auscultatory signs in the chests of children with miliary tuberculosis. If the lungs are involved, there is one type of râles that is peculiar to this condition—a small, high-pitched, subcrepitant râle that is uniform throughout the lung fields. Occasionally these

râles occur early in the disease and persist throughout its course. We see the type of well nourished and developed children that are seen at the Children's Memorial Hospital rather less frequently than children with marked involvement for whom the prognosis is serious when the patients are first observed.

DR. LEVINSON: Replying to Dr. Krost, we used the tuberculin for the Mantoux test in 1:1,000 dilution, which should be sufficiently sensitive. We tried the Moro test as well, but the reaction was not as clear-cut as the Pirquet.

There is no question about the great difference in the material at the Cook County and other hospitals. Most of our cases occurred among Mexican or Negro children. I think race is not as great a factor, however, as is the hygienic environment. Many of our cases were diagnosed, or at least proved, by necropsy. We believe that tuberculosis should never be diagnosed on roentgen-ray observations or on history alone, but on a combination of history of contact with tuberculosis, physical examination and roentgen-ray observations. In many instances, we were given a history of measles and whooping cough immediately preceding the tuberculous process.

We have seen only three cases of pleurisy with marked effusion, but in some instances a small amount of fluid has been found at autopsy. We have also had some cases of thickened pleura.

Cases in which tuberculous meningitis is not an end-process of a generalized miliary tuberculosis are rare. I do not know of a single case that came to autopsy in which we did not find generalized miliary tuberculosis.

I agree with Dr. Blatt regarding the presence of fine, crackling râles in most cases of miliary tuberculosis, but I have never been able to convince myself that the râles found in miliary tuberculosis are different from those in other conditions of the chest. On many occasions we have not found definite symptoms in the chest, but the cases have been proved to be miliary tuberculosis.

AMAUROTIC FAMILY IDIOCY, TYPE TAY-SACHS: A CASE WITH A PROTRACTED COURSE. GEORGE B. HASSIN and ARTHUR H. PARMELEE.

This paper will appear in full in a later issue.

DISCUSSION

DR. GERSTLEY: Recently I saw a new-born baby in our maternity ward. Possibly the mother was the one that Dr. Parmelee saw, although in this case the mother's intelligence was limited, and she was extremely uncooperative. Two previous children had been amaurotic family idiots, but both were now dead. Her neighbors had attributed the disease to her breast milk, and she had insisted on weaning the new-born baby immediately.

Examination showed a child of normal size and nutrition; nevertheless, the facial appearance was not that of the average infant. The skull verged on oxycephalus. The eyegrounds were normal; the reflexes, particularly the knee jerk, were brisk. I am attempting to keep this child under observation, and as we are fortunate enough to have Dr. Hassin who has studied this disease so extensively, I would like to ask him for suggestions as to any special means of diagnosis in so young a patient.

DR. BRENNEMANN: Ten or twelve years ago, I saw a case in a child, 2½ years of age, who lived to be 4. Dr. Brown Pusey said there was a typical cherry-red spot. Spasticity and convulsion increased in that child. It did not look like a typical case of amaurotic family idiocy, but I wonder whether it might not have been of the type Dr. Hassin has discussed. I would like to know whether he considers the cherry-red spot pathognomonic.

DR. PARMELEE: I am sure that the patient Dr. Gerstley mentioned is not the same woman to whom I referred. My patient is intelligent, and so far as I know, the second child is not yet dead.

One thing I wish to add to the clinical report which my diagnostic acumen did not permit me to place on the first report. The child had many things suggestive of decerebrate rigidity, which has been so well described in previous cases reported by Dr. Hassin. When the head was moved to one side, the movements of the arm and leg were different from those produced by pushing the head to the other side. Evidently there was a degenerative process that involved the entire central nervous system, but the idea of amaurotic family idiocy did not occur to me until the ophthalmologist made his report—that if the red spot had been present, the optic atrophy and the peculiar appearance of the macula would have suggested amaurotic family idiocy. I then studied the case with that idea in mind.

Regarding the positive globulin test, it seems to me that with the rapid destruction of brain tissue and the marked changes in the pia-arachnoid, there was enough change to produce the positive globulin test.

DR. HASSIN: The complete paper to be published in the AMERICAN JOURNAL OF DISEASES OF CHILDREN contains answers to the majority of questions asked. As to the changes in the spinal fluid the interpretation as given by Dr. Parmelee is correct, and I agree with him.

The case under the observation of Dr. Gerstly should be studied in reference to the phenomena of decerebrate rigidity described in some cases of this disease, including one by myself. In my case, the so-called Magnus-de Kleijn phenomenon was marked: turning of the head to the left, for instance, caused marked extension of the left extremities accompanied by marked flexion of the opposite extremities and vice versa.

Another condition to be watched for is that of epilepsy, complete or incomplete, which is frequent in amaurotic family idiocy. In the presence of phenomena of decerebrate rigidity, epileptiform states may settle the diagnosis even in the absence of the cherry-red spot which is considered, in my opinion unjustly, essential in the diagnosis of this disease.

PEDIATRIC SECTION OF THE NEW YORK ACADEMY OF MEDICINE

Regular Meeting, Jan. 12, 1928

WILLIAM ROPES MAY, M.D., *President, in the Chair*

ENDOCRINE GLANDS IN RELATION TO INFANCY AND CHILDHOOD. DR. LEWELLYS F. BARKER.

This paper is published in full elsewhere in this issue.

DISCUSSION

DR. GEORGE DRAPER: There are two or three things that this paper has brought to our attention which can be mentioned briefly; in the first place, the great restraint that should be exercised in the interpretation of endocrine effects, and the intense demand that it puts on all for accurate clinical observation.

It is interesting also that Dr. Barker should have called attention to the fact that during the period of growth and development there is a dual function of the endocrine mechanism. I think that this is often lost sight of. The glands not only are engaged in the task of driving the young organism forward to completion, but they are concerned with the day to day metabolism

balances which are under their control. Consequently, during this early period they are subjected to a much more violent demand than in later life. When growth stops and development ceases, one can imagine that their task changes considerably.

The remarks about the pituitary gland called attention to the fact that it is possible for a person to have all the symptoms of pituitary disease without disease of the gland. The work of Frankl-Hockvart points out that when there was pituitary insufficiency due to tumors the genital dystrophy and accumulation of fat were of almost constant occurrence. In collecting material as evidence for this statement, he found to his astonishment that at least sixteen of his patients were underweight. So that Dr. Barker was wise to emphasize the point that while these conditions are called pituitary syndromes, they may not be.

But it seems to me that the most striking feature of his discourse was the implication that pediatrics and general medicine are one and the same thing, that the problem of adjustment of a living organism to environment is being dealt with. Though it may interest some to occupy themselves with one end of life, some to occupy themselves with the middle portions, and others with senescence, the principles are the same. Perhaps the most important, most significant aspect of Dr. Barker's remarks was the general implication that whether one is a pediatrician or an internist, as long as one is a clinician and is studying the problems of adjusting the living organism to its environment, one will use as fast as it is prepared for him such information as is truth about the endocrine glands.

Dr. Charles R. Stockard: As Dr. Barker brought out and as Dr. Draper emphasized, the discussion of endocrinology before people interested in diseases of childhood is particularly appropriate, because in that stage of life the actions of these glands have the most marked influence. They really have a much more important influence in effect than they may have at any other time, because a disturbed internal secretion in a child not only causes disease or discomfort but actually modifies his growth and development and future condition in life. It would be impossible for such a disease or disturbance to do this to an adult, a finished individual.

In considering the parathyroid glands, I was interested to hear what Dr. Barker said in regard to the difficulties of being certain in many cases that a disturbance of the parathyroid was actually causing certain conditions which, offhand, one readily attributes to disturbances of these glands.

We have been working for a few years on the effects of these glands on the growth of different animals, especially on calcium or bone growth, calcium metabolism. And Dr. Nonidez has found, especially in chickens grown in the absence of violet light or blue light although fed on the antirachitic diets, that these animals not only developed rickets but later, in many cases, died of tetany. When the parathyroid glands of such animals are studied they are found to be completely modified and to have undergone a mucoid degeneration. So one might say that the real condition that the chicken has or dies of, finally, is tetany, with a complete degeneration or absence of this gland.

In dogs, unfortunately, I have had a good deal to do lately with the condition of tetany which has manifested itself in a most peculiar way, in what is known as running fits or fright and nervousness. This is a typical reaction which is much like tetany in certain of its phases. At any rate, a dog dies of it after removal of the parathyroid gland. But in other cases the tetany is brought on by toxins absorbed from intestinal parasites such as hookworm, threadworm or *Trichocephalus*. If a dog is infested with either hookworm or *Trichocephalus*, it goes into a slight tetany. The calcium is low and when the calcium is raised or when the animal is treated with bromides, etc., the condition can be corrected temporarily as Lampson has recently shown. However, he can be completely cured by removing the parasites.

In regard to change in the parathyroid in such conditions, I have not obtained evidence bearing on it, because the only parathyroids secured from such animals have seemed to be histologically normal. However, this brings out, in a way, and stresses the point that Dr. Barker made, that many of these disturbances of the glands or certain symptoms connected with their disturbances may be largely environmental. It may be the influence of environment acting on glands rather than any innate defect or disturbance in this gland.

Dr. Barker emphasized the fact that there is a strong question as to whether the thymus is a gland of internal secretion. Of course that is a point about which I should like to be just as cautious. However, from a development standpoint, from the standpoint of children and young animals, I think that one should realize that whenever the thymus is unusually large or persistent in its presence and size, one must remember that this is a symptom of arrested development, that the involution of the thymus is just as much a proper step in growth and differentiation as the development of the gonads or the arrival of puberty. So that when any person has a large or persistent or infantile thymus, one naturally expects to find bad gonadal conditions or undescended testes and other things that might be correlated situations. I do not know of any real, cleancut case of defect attributed to an actual thymic cause that might not be interpreted as a correlated thing associated with the arrest of development of which the presence of thymus is merely another symptom.

In the case of the pituitary gland, Dr. Barker brought out the fact that there is a rareness of acromegalia in children which, of course, one appreciates. But it is interesting to know that there is a group of animals which has been frequently studied and experimented with that shows acromegalia during early stages in certain breeds or varieties, and that is in the common dog. The St. Bernard dog really has acromegalia in several noticeable conditions or ways as a young pup; therefore one might almost say that it is born acromegalic. Hence it is favorable material for studying the early conditions or onset of acromegalia in a young, apparently normal animal. It is considered normal by a layman or by persons who do not appreciate that part of it. In these animals one accidentally finds a most interesting connection between the pituitary and the gonadal development and also a more interesting connection — the relationship between the pituitary gland and the function and development of the kidneys.

Recently, I have examined four litters of pure hybrid pups, the offspring of St. Bernard dogs and a large and normally gigantic dog, a Great Dane. Many of these pups have had defective kidneys, and in almost all of them this defect has been so exaggerated as to be fatal, the dogs dying shortly after birth of an extreme hydronephrosis in both kidneys. They not only show this condition, but a peculiar thing happens in pups produced by the male Great Dane on the female St. Bernard. Then the sexes differ in their reaction, apparently in the females, so far as their sexual development is concerned, the internal genitalia are normal. But the males have undescended testes, which are high and lie beside the kidneys. Instead of developing a normal duct of the testes, the males have a typical uterus in their arrested state similar to the internal genitalia of females. But on making a reciprocal cross, this apparently does not occur. The male development apparently is almost normal, although none of the animals have reached maturity, so that their fertility cannot be determined.

In the case of undescended gonads and hypogenital syndromes of different kinds, as is brought out distinctly, these are constantly and frequently associated with other disturbances, and in one group of dogs sterility is prevalent. It is hard to say in what percentage it actually occurs, but it is really surprisingly high, in fact discouragingly so, if one attempts to breed such animals. This is true among bulldogs, which certainly have defective conditions of the pituitary glands as well as defective conditions of the thyroid. They frequently have undescended testes, and one might almost say are generally sterile.

In all these conditions and in rickets as well, or in faulty metabolism and formation of bone, there has been a decided difference between the way in which the male and the female act or grow. In rickets, the male is always more severely affected than the female, so that in a litter of six pups, in which there might be three males and three females, the three females will develop in a normal fashion and the three males will have decided rickets when brought up under identically the same conditions. In the case of the St. Bernard and the Great Dane, it is easy to rear a normal, strong, well developed female. Her bony development is good, and she is strong and wide in the hips and flanks, whereas it is difficult to rear a normal, well developed male. The defect is largely located in the bones, so that it is difficult to rear a male St. Bernard with strong hips and well developed hind quarters.

I am inclined to believe, with little human evidence, although there is some, that study would show, very likely, that there is considerable difference in calcium metabolism and ability of the female to form bone from that found in the male.

DR. FREDERICK TILNEY: In his summary, Dr. Barker called attention to the fact that the clinician has played an important rôle in the revelation of the endocrine system. He has shown that the clinician has been a pioneer in discovering this system. He has also shown that in many instances the clinician has been a rather overzealous advocate, and he also indicates that the physician is to be the leader in this field in the future.

The clinician, it seems to me, has another office to fill in this department of medicine. He must be the final judge concerning the glands of internal secretion, certainly in all matters pertaining to their practical application. He must avoid that somewhat impetuous enthusiasm of advocacy. He must see these glands in their true proportions and relations in the entire realm of internal medicine. He must cultivate, as he has cultivated, an attitude of healthy skepticism in a field which tempts the fancy so much and invites also to romance. I myself, must admit to an attitude of not a little skepticism. This may be due, perhaps, to the fact that I have not had any intensive experience in glandular therapy. But I think it is also due to a rather extensive experience in the morphologic aspects of these glands in many different forms in vertebrates.

Dr. Barker's review stimulates me to think more particularly about the glands connected with the brain, that is the endocrine glands connected with the brain, and briefly to review the status of the present knowledge concerning these glands. Take, for example, the case of the pituitary gland. The old ideas about the anterior and the posterior lobes of that gland are now recognized as wholly inadequate to meet the morphologic and physiologic requirements in the consideration of this part of the body. More recent analyses of the pituitary gland in man and the pituitary gland in general throughout the vertebrates show that it probably is made up of three glands, at any rate, of three distinct glandular portions that differ from each other histologically and probably function in different ways.

This difference in the character of the pituitary gland varies considerably with different animals, and this variability, I think, influences the therapy. For example the part of the sheep which is usually spoken of as extract of the posterior lobe contains an enormous addition of glandular tissue which is found nowhere outside of the ungulates. And the pharmacologists are saying that they are giving posterior lobe when they are not giving that at all; they are giving an enormous extract of the glandular tissue derived from the buccal cavity. So that, depending on the species used for the preparation of extract for therapeutic purposes, great differences arise, and there is great discrepancy of opinion in the users of various makes of extracts.

This arrangement of the pituitary gland accounts, I think, for the difference of opinion concerning the results of experimental extirpation. I am certain that it is impossible to remove the glandular portion of the pituitary in toto. To do so could not fail, particularly in experimental animals, to strip off the

nervous portion and in many species to open the third ventricle and thus injure the tuber cinereum, the part of the brain which is coming in for more consideration as an important functional area, as experience increases.

The classification of syndromes, of which Dr. Barker spoke, is in that dogmatic state of almost too cleancut diagrammatic description. As time goes on, these syndromes will be seen to merge one into another and to have none of this cleancut diagrammatic appearance which they seem to have now. The condition is very much in the state that aphasia was a few years ago when every neurologist had his own pet diagrammatic theme for the explanation of aphasia. So with these syndromes of disease of the pituitary gland almost every enthusiast for it has his pet scheme and classification of the constitution complexes constituting the various symptomatic entities.

Dr. Barker has mentioned the question of the tuber cinereum, which has been shown experimentally to produce a great many of the symptoms which enter into the pituitary syndromes. Consequently, one shall have to be slow in coming to final decisions as to just what the function of the pituitary body is and how much of what is attributed at the present time to glandular activity of this buccally derived gland may not be attributed to this basal portion of the diencephalon.

I cite these facts merely to indicate on how many points our knowledge is still deficient and how wise it is for one still to withhold anything like the final decision, or to be dogmatically conclusive.

I was interested in Dr. Barker's references to the parathyroid gland. My experience with that gland has been extremely limited, but Dr. Barker's paper brought out from Dr. Stockard some observations with reference to calcium metabolism in dogs which he has had under observation and the remarkable changes produced in these animals in consequence of calcium, changes in calcium metabolism, and the running fits, those peculiar attacks of distemper which he observed in a dog suffering from infection in the intestinal canal. Up to the present, in the laboratory, I have seen many of these symptoms which have been looked on as encephalitic manifestations, and yet when the brains of these animals were examined little was found to indicate the presence of a gross or extensive inflammation. This observation of Dr. Stockard's has given me an increased confidence in the belief which I have had for some time past in the encephalitis which is now seen. Whether it is the epidemic form in man or one of the various other varieties of so-called infection of the brain, the inflammation of the brain is in all probability not due to a direct infection of the brain itself. For a long time, I have felt that the brain in encephalitis does not pathologically present the appearance of an organ which has suffered from a direct assault from bacterial infection. To me, it looks much more like the results of toxemia. For some time, I have been thinking that the main infection in encephalitis is either in the upper respiratory tract in general or in the intestinal canal and that in dealing with the treatment of this disease attention has been directed almost exclusively to the brain; whereas the offending source, the focus of infection, is probably not in the brain at all but is either in the respiratory tract or in the intestinal canal or in some other focus of infection which is extraneural.

It is not generally known or realized what an indomitable tendency the brain has for the development of glands. One thinks, when one thinks at all of the brain in connection with glands of internal secretion, of the pituitary gland. The pituitary is only a small part of the story. And the significance of this tendency for the brain to develop glands and the reason for it are not understood at present, yet there must be some important phyletic explanation back of it. If one considers all of the various types of vertebrate that one knows from this standpoint, it is possible to identify and recognize in the brain eleven glands, all of them of internal secretion. They are, of course, variable in their appearance. Few vertebrates possess all of these eleven glands at one time, though one class does. And the combinations in which these eleven glands of the brain occur is very different.

The most constant of these glands are the epiphyses which are spoken of as the pineal glands. A new gland has recently been described in connection with the brain which I have taken the liberty to call the metaphysis cerebri. It is an enormous structure and has all the appearances and histologic characters of blood glands. One of the members of the staff in the laboratory has spoken of it as the brain tonsil. It looks not unlike tonsillar tissue in many of its features.

Each one of these glands plays some special part in the metabolism of the animal in which it occurs, and when a number of them are present simultaneously they must play more or less in harmony with each other. So I feel that it is difficult to consider any one gland, whether it is the hypophysis or the epiphysis, out of its biologic setting, that is, separated from and apart from its relation to all of these other glands whether they appear very rudimentary in early development or whether they appear fully developed in adult life.

I should like to call attention to a gland that for some reason Dr. Barker did not mention. Perhaps he feels that all the antagonism which it has aroused because of the conflict that is going on about it justifies its omission as a gland of internal secretion. But it is somewhat of a pet of mine, and I have thought about it and worked with it for some time and I should like to consider the evidence that the epiphysis is really a gland of internal secretion. It may be that because this gland goes to a point of development where it contains a great deal of brain sand and has other appearances of a degenerate state that it has little glandular activity, but that, it should be borne in mind, is at a late stage of its history. In childhood and infancy the epiphysis has every appearance of a gland of internal secretion, and I fully believe that in those stages of life it is an active gland of the endocrine type.

Viewing it from another standpoint, from the standpoint of its comparative history, I cannot conceive how there could be any doubt as to its actual glandular character. It is known that in birds, for example, the epiphysis develops a duct and ample connections in the enormous racemose gland, so that its secretions may be delivered to the third ventricle, and are delivered to the third ventricle. This also holds true in many reptilian forms, and it is certainly true in the amphibians and in many of the fish. So that the history of this gland, the epiphysis, is sufficient to aline it in the class of endocrine organs.

This brings up an interesting consideration; namely, the syndrome of childhood that Pellezzi described in 1912, a condition in which the young child begins to grow very rapidly. The long bones grow; sexual differentiation occurs so that a child of 6, 8 or 9 years may have the stature and the sexual differentiation of the full grown adult. Pellezzi found this to be due to a change in the pineal gland, the epiphysis, such a change as inhibited the action of its large cells and destroyed the gland. He came to the conclusion that the function of the pineal gland in man particularly, but also in other animals, particularly mammals, was to hold in check the action of the pituitary gland and thus to further a longer period of maturation, that is, to retard the differentiation of the individual in both growth and sexual specialization.

This syndrome has been disputed. It is a matter of much debate and doubt today and probably rightly so. And yet it seems almost too casual to dismiss the possibilities of this gland acting in the manner which I have indicated simply by saying that the tissue of the pineal body in adult life has all of the appearance of a degenerate organ.

I should like to say a word about the endocrine glands in determining the psychic constitution. Doubtless there may be some grounds for believing that the glands of internal secretion do play a part in psychic tempo, but to say that they determine in any decisive manner the psychic constitution is, to my mind, overlooking many important facts about their function and their morphology. According to that conception, the psychic constitution of the elephant, the horse, the cow,and in fact of all ungulates ought to be infinitely greater than that of a man because, in proportion to the weight of the brain the pituitary body and the pineal gland of the ungulates and the proboscidians are greater

than in man. In accepting this conception, one is slipping back into the old attitude of humoral medicine, back to the days of Descartes when that philosopher thought that the seat of the soul was in the pineal body. It seems to me that this point of view overlooks entirely perhaps the greatest gland in the body and I think it may be justly called so—this gland is the brain, which after all contains the basic material out of which the psyche may be constructed, and which does not require even the subsidiary consideration of such lesser satellites as the glands of internal secretion.

Nor must it be overlooked or forgotten that the endocrine glands themselves are at best and at most part of the general systemic circulation. They contribute to the blood their specific secretion, but they depend on the blood for their existence. They have no despotic autonomy. They are subject to the chemical influences which affect the entire constitution generally. The great multitude of factors which act on the blood also act on the endocrine glands. Like other organs of the body, they illustrate the tetroplastic theory of action, reaction and interaction. They do not motivate evolution; they do not of themselves explain psychic constitution, nor do they afford any exclusive therapy even in their own domain.

If I have seemed to voice a considerable degree of skepticism, it is only because all of these doubts which I have expressed are really problems in my mind, problems perhaps in all of our minds, which open this field still further in our efforts to determine the truth concerning this subject which is so interesting and which has been such a fertile field in the revelation of biologic facts. A great debt is owed to those who by their enthusiasm and their courage have acted as pioneers and who today stand out with pronouncements and declarations concerning the glands of internal secretion which may seem far to outrun common judgment, but which after all cannot fail to be extremely stimulating and which should be of greatest service in the further exploration of the endocrine glands.

NORTH PACIFIC PEDIATRIC SOCIETY

Jan. 28, 1928

R. J. Miles, M.D., *President, in the Chair*

Hare-Lip and Cleft Palate. Presented by Dr. Coe.

Dr. Coe advised operation of the lip when the baby weighs 12 pounds (5.4 Kg.) and closing of the soft palate as soon as a good recovery was made. The hard palate should be closed later. In two cases which he reported he used a Logan traction bow and paid scrupulous attention to keeping the lip wound clean following the operation.

Sinusitis in Children. Presented by Dr. Houston.

A boy, 6 years of age, had had copious nasal discharge and obstruction, fever, nausea, anorexia and pain. (Symptoms in some cases are cough asthma, albuminaria and edema.) This boy had had his tonsils and adenoids removed two years before presentation, without relief of symptoms. Dr. Houston believed the commonest cause of sinusitis is disease of tonsils and adenoids and that removal of the tonsils and adenoids is followed by cure in 90 per cent of the cases. The boy was cured by a radical operation.

TUBERCULOSIS OF THE SPINE IN YOUNG CHILDREN. Presented by DR. EIKENBARY.

Dr. Eikenbary emphasized the fact that the most important part of treatment is prolonged recumbency on a frame. He advised seven or eight months, until the greatest possible correction is obtained, then a fusion operation followed by the wearing of a brace. He also presented some cases of poliomyelitis. The after-care consists of rest with necessary support until all soreness is gone; later, muscle training is added. Electricity is not used. Dr. Eikenbary also presented a patient who had had the condition for three years. Arthrodesis of the right shoulder had caused the right arm, at one time useless, to function well, permitting practically all movements.

ACUTE INTESTINAL OBSTRUCTION (2 CASES). Presented by DR. SOMMER.

An infant, aged 2 days, weighing 8 pounds (3.6 Kg.) presented the usual symptoms of complete obstruction. A large pouch near the iliococeal valve was found on operation by Dr. Coe. The baby died. A second case was also that of a newly born child; the baby died. Postmortem examination showed a constriction about 6 inches below the pylorus.

CELIAC DISEASE. Presented by DR. SPICKARD.

A boy, aged 5, was admitted to the Children's Orthopedic Hospital when he was 3 years old. The weight at that time was 23 pounds (10.4 Kg.). He was given a diet of protein milk for some months; then cottage cheese, ripe banana and meat were added at intervals. Insulin was given at times and proved of value in stimulating the appetite. The patient gained 5 pounds (2.3 Kg.) the first two months. He had the usual susceptibility to colds and still had a relapse at times. Vegetables and orange juice were given to him at times. He had had a few relapses due to taking food from other children's trays. The best gains were made on a restricted diet.

DISCUSSION

DR. SPOHN: There is probably no dextrose intolerance in some cases, and insulin is thus not indicated in these cases.

LYMPHATIC LEUKEMIA. Presented by DR. SCOTT.

A boy, aged 12, complained of weakness, pallor, epistaxis, large spleen and enlarged lymph glands. He was treated with benzene, 5 minims (3 cc.) three times a day without improvement. Roentgen-ray treatments caused marked improvement in the white count and in the size of the spleen and glands. He continued to have hemorrhages in spite of transfusions. The question was raised whether the effects of the roentgen-rays have any real influence on the progress of the disease. At autopsy, a very large thymus was found. He received, in all, seven or eight roentgen-ray treatments, with marked reduction in the white count and in the size of the spleen. He was always quite toxic after roentgen-ray treatment.

ERYSIPELAS. Presented by DR. REMBE.

A child, aged 6, had a temperature of 106 F. on entering the hospital. She was given antitoxin, and magnesium sulphate solution was used locally. She developed a number of large abscesses in the muscles, and these were opened and drained. Later she developed a rapid, irregular heart with murmurs and a generalized edema. She lost many of her first teeth. Later treatment consisted of repeated transfusions of whole blood, dextrose solution and intra

peritoneal injections of citrated blood. Digitalis, 6 cc. in twenty-four hours, was given for the cardiac failure and apparently met the requirement as the rapid irregular action ceased. The ultraviolet light was used and believed to be of value. The child is now apparently in good health, but still has an enlarged heart.

A Case for Diagnosis. Presented by Dr. Smith.

An infant, 5½ months of age, was admitted to the hospital with an obvious mental defect. He had marked snuffles. He was growing, but remained thin. The Wassermann reaction of the blood was negative. Thyroid therapy did not prove of benefit.

Edema. Presented by Dr. Deever.

A child, 3 years of age, had edema. Medication decreased the condition, but it recurred. Ammonium nitrate was given most of the time. The edema persisted.

DISCUSSION

Dr. Smith: In order to cure patients who have nephrosis, it is important to clear up foci of infection.

Poliomyelitis. Presented by Dr. Herbert Coe.

For purposes of treatment, Dr. Coe divided the course of the disease into three periods: (1) the acute stage, (2) period of improvement and (3) period of permanent paralysis. During the acute stage, pressure is reduced by lumbar puncture or the use of salines. Later in this period he advocated continued rest and preservation of muscle balance (avoid stretching of muscle). Electrical reactions are useless for testing muscle power, but are a good test for voluntary power. Heat is of value: radiant heat, whirlpool bath and perhaps diathermy.

In the second period, muscle training should be employed. Voluntary movements should be made by command, the child using his conscious control. Fatigue should be avoided. First easy movements, then gradually more difficult movements should be made. Accuracy in the use of the individual muscles should be insisted on. Mental concentration is necessary. There must be a rest period daily. The development of paralyzed muscles depends on the development of collateral nerve paths. Activity should be restricted. Quoting Dr. Lovett: "Weight bearing with or without braces during the first year is risky." There may be decrease of strength in the third or fourth years, but usually this returns with care. Dr. Coe stressed the importance of preserving a good mental attitude in both the patient and his family.

Multiple Juvenile Diabetes. Presented by Dr. C. Luverne Smith.

The father of one group had had diabetes for two years. All the children were on a weight diet and doing well. Not all, however, were receiving insulin. Dr. Smith said that in feeding young diabetic patients the dextrose-fatty acid ratio should be about 1:1 to prevent ketosis.

DISCUSSION

Dr. Spohn: I suggest using sufficient dextrose and insulin to maintain growth.

Some Practical Points in Treatment of Undescended Testicle. Presented by Dr. J. Tate Mason.

According to statistics from the World War records, this condition was found in 3.1 per cent. There are several embryologic factors, but an important

one is the blood supply. The arteries are often insufficiently long to permit descent. Attempt to bring the testicle down by operation often destroys some blood supply and results in partial atrophy. Treatment by gentle traction, beginning as early as possible, is the best method. Dr. Mason discussed methods. If the patient is not cured of the condition, operation should be performed toward puberty. If operation does not cause cure, the offending gland should be removed to prevent sarcoma. The author showed slides to illustrate embryologic development and methods of treatment.

Possible Factors in the Etiology of Epilepsy and Allied Conditions in Children. Presented by Dr. George Swift.

Dr. Swift made a plea for early recognition of the preconvulsive stage, for it is too late to get good results after mental deterioration. There are many theories regarding etiology, toxic, traumatic, etc. Is there a potential epileptic condition? May this be due to defective development of the cranial cavity? It is possible that such defective development may permit pressure on the sigmoid or inferior petrosal sinus, thus increasing intracranial pressure. The operation devised by the author is for the purpose of relieving such pressure. Dr. Swift believes that he has had some encouraging results.

Obstruction and Cause of Persistent Urinary Infection in Children. Presented by Dr. H. B. Heppler.

Pyelitis as an entity does not exist. The entire urinary tract may be invaded. In pyelitis of the new-born, the relative incidence is as great in boys as in girls. It is usually due to pyogenic bacteria. From 1.5 to 2 per cent of all children have some anomaly of the urinary tract. These constitute the persistent cases in which the condition will clear up only by cystoscopic treatment. Dr. Heppler showed slides to illustrate various congenital anomalies. If the condition did not clear up after about three months' intensive treatment, he advised cystoscopy.

Intussusception. Presented by Dr. Wilbur Graham.

Dr. Graham discussed a case of intussusception complicated by the congenital anomaly of incomplete rotation of the intestines. He showed slides and discussed in detail the embryologic development of the intestinal tract.

Some Factors of Interest in Preventive Orthodontia. Presented by Dr. W. R. Dinham.

Dr. Dinham made a plea for early recognition of the need for corrective measures. After malocclusion has occurred, it is difficult to get a good correction. He believes that dietary defects are factors in improper development of the teeth. He showed slides illustrating several abnormal conditions.

Congenital Vascular Nevi (with Cases). Presented by Dr. Henry Odland.

This condition is more frequent in females, occurring in thirteen of sixteen cases. The portwine mark is the most difficult to cure. Radium and roentgenotherapy may be used. The employment of the Kromayer lamp has proved disappointing. Angiomas yield to radium or roentgenotherapy. Hot water treatment is often unsuccessful and is dangerous. Radium is advised, as it is painless and produces the best cosmetic results. Short repeated exposures are advisable. Younger patients respond better than old. To avoid telangiectases, heavy doses of radium should be avoided, and appropriate filters should be used.

DISCUSSION

DR. SPOHN: I would advise the use of carbon dioxide snow for economic reasons.

ERYSIPELAS IN THE NEW-BORN. Presented by DR. ARTHUR H. GRAY.

The prognosis is bad, especially in artificially fed babies. The disease is not so common as formerly, owing to improved obstetric technic. Dr. Gray discussed methods of treatment and said that the breast-milk feeding was imperative.

Book Reviews

DIE BRONCHIEKTASIEN IM KINDESALTER. By O. WIESE. Price, R. M. 12.90, bound, R. M. 15. Pp. 116, with 86 illustrations. Berlin: Julius Springer, 1927.

Recent advances in pulmonary surgery and improved methods of roentgenography have given a marked impetus to the study of chronic conditions of the lung of a nontuberculous nature. A monograph such as the present one on bronchiectasis during childhood may therefore be expected to receive a cordial reception in the pediatric world. Despite the sympathetic attitude, however, the present work is not entirely satisfactory, due to a rather poor arrangement of the text and an incomplete discussion of the author's own material. There is an impressive total of 114 cases in the present study, but it requires a reading of almost the entire monograph to glean the essential observations.

There is an excellent discussion of the pathologic changes in the acquired, as well as in the so-called congenital bronchiectasis, and the text is appreciably enhanced by well selected illustrations. The clinical diagnosis, too, is handled in a thorough manner, but suffers somewhat from too many references to the opinions of others. Perhaps the most important point brought out in the differential diagnosis is the contrast between the marked changes in percussion and auscultation, and the relatively slight evidence of abnormality in the roentgenogram. Excellent roentgenograms are shown before and after injection into the bronchi of one of the preparations of iodized oil. The technic for such injection as performed by the author was as follows: Small doses of potassium iodide are given to the child several days previous to the injection, to discover a possible idiosyncrasy to iodine. The child is then given a sedative, and the pharynx and entrance to the larynx are anesthetized with 10 per cent cocaine solution. A few drops of this solution are also dropped into the larynx and trachea. A rubber catheter, stiffened with a silver wire, is now passed between the vocal cords down the trachea into the right or left bronchus as desired. The position of the catheter is verified by fluoroscopy, and during the fluoroscopic examination, warm, 40 per cent solution of iodized oil is injected slowly. A roentgenogram is then taken as quickly as possible, since the paroxysm of coughing, which usually ensues, scatters the oil into all the bronchi and may defeat the object of the injection. Danger of cocaine poisoning during this procedure was said to be relatively slight.

UNDERSTANDING HUMAN NATURE. By ALFRED ADLER, M.D. Translated by WALTER BERAN WOLFE. Pp. 286. New York: Greenberg, Publisher, Inc.

Any physician interested either in mental medicine or in pediatrics, and all family practitioners who so frequently have to deal with family situations should be acquainted with the work of Dr. Adler.

The preface to this volume is a bit of selling talk, prejudicial to a reader skeptical of claims of interpretations and discoveries of secrets of nature. Many statements which occur in the text of the book are of a dogmatic nature claiming to settle questions of human conduct. Some of these questions have interested thinkers from the beginning. One feels that the answers to these questions are claims; they are stated in simple terms, but frequently the reviewer was left with a feeling that the explanation was much more superficial than the claim. In many places most important truths are stated with great assurance as if proved in an engagingly simple way. In fact, the one criticism is that claims of proof are freely indulged in on what seems an insufficient basis. Some of the chapter headings suggest what is meant by this comment; for example, chapter 1, The Soul; chapter 6, The Preparation for life; the title of book 2, The Science of Character. In chapter 6, The Prepara-

tion for Life, is treated under the headings: Play, Attention and Distraction, Criminal Negligence and Forgetfulness, The Unconscious, Dreams and Talent. This gives the feeling of a coat of many colors.

The genesis, or the reason of being of three types of problem children—the child with organ inferiority, the spoiled child, and the hated child—is interestingly discussed. The development of an inferiority feeling is handled in a manner that is far from convincing. The idea that all psychic efforts and conduct are directed consciously or unconsciously toward a certain goal is insisted on. It forms an extremely important element in Adler's consideration of human conduct. Sex is decidedly subordinated to egoistical drives toward power. The chapter headings are: Book 1, The Soul; Social Aspects of the Psychic Life; Child and Society; The World We Live In; The Feeling of Inferiority and the Striving for Recognition; The Preparation for Life; Sex; Family Constellation. Book 2, General Considerations; Aggressive Character Traits, Non-Aggressive Character Traits; Other Expressions of Character, and Affects and Emotions.

CULTIVATING THE CHILD'S APPETITE. By CHARLES ANDERSON ALDRICH, M.D. With a foreword by CLIFFORD G. GRULEE, M.D. Price, $1.60. Pp. 127. The Macmillan Company, New York.

Pediatricians have stated that the most common complaint today is the unsuccessful effort on the part of mothers to overcome the child's apparent lack of appetite. A majority of the families who have an abundance of food, and in whom the parents are striving to give a maximum amount of what they consider a well-balanced dietary, find that it is impossible to get the children to eat what it is thought they should. Aldrich, in this little book, discusses the nature of hunger and appetie, his conception of the hunger-appetite reflex, the psychologic and physiologic factors which influence it. He believes that prevention of such disturbances is more successful than the treatment in the established case.

This volume is helpful to mothers especially as among other things it discusses methods of getting the child into the habit of eating. Fathers who read this book will learn the uselessness of indulging in a combat with the child for refusing to eat. The writer urges us to forget about calories and the objective of a maximum weight, the essential being that the child should make a proper yearly increase and should develop according to his individual needs. Pediatricians are familiar with such cases, but they will enjoy the author's experiences and the advice which he gives. Undoubtedly the psychologic factor is of most importance in the causation of this common type of anorexia and the treatment is likewise psychic. Each patient should have a thorough physical examination, and the physician can well reinforce his advice by recommending that the parents read this useful book.

THE POLYNUCLEAR COUNT. W. E. COOKE, M.D., and ERIC PONDER, M.D., D.Sc., with an Introduction by JOHN HAY, D.L., M.D. Price, $3. Pp. 79, with 2 plates. Philadelphia: J. B. Lippincott Company, 1927.

This book is concise and well written. The authors outline their work in simplifying the Arneth count, as an adjunct to the clinical studies of many diseases. The first chapter is devoted to an explanation of the differentiation of the polymorphs according to their nuclear configuration. The second chapter deals with the polynuclear count in health, and the third to the count during the infective state of the disease. The final chapter takes up the study of the macropolocyte, and an appendix takes up the various staining methods in full.

The utility of the count as an adjunct to the clinical methods in diagnosis will be obvious to the reader. Its value in diagnosis lies in the fact that if the count is dislocated to the left, the patient is in the infective state. Having that point definitely settled is of great assistance to the clinician, and the search for the focus of infection can be undertaken with the confidence that one exists.

SYSTEMIC AND FOCAL IMMUNIZATION THROUGH IRRADIATION. S. PESKIND. Pp. 30. Cleveland: S. P. Mount, 1928.

In this monograph, a hypothesis is developed by the author explaining the action of ultraviolet light in developing immunity. A section of skin or mucous membrane after irradiation with ultraviolet light becomes an antigen trap or filter. The formation of antibodies in infective states is explained by the absorption of germ antigen by irradiated skin.

Directory of Pediatric Societies

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SECTION OF DISEASES OF CHILDREN

Chairman: Dr. Hugh McCulloch, 500 S. Kingshighway, St. Louis.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Minneapolis. Time: June 11-15, 1928.

AMERICAN PEDIATRIC SOCIETY

President: Dr. J. Claxton Gittings, 1828 Pine St., Philadelphia.
Secretary: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: Washington, D. C. Time: April 30 to May 2, 1928.

THE ASSOCIATION OF AMERICAN TEACHERS OF THE DISEASES OF CHILDREN

President: Dr. J. P. Crozier Griffith, 1810 Spruce St., Philadelphia.
Secretary: Dr. Paul W. Emerson, 86 Bay State Road, Boston.
Place: Minneapolis. Time: June 12, 1928.

AMERICAN CHILD HEALTH ASSOCIATION

President: Hon. Herbert Hoover, 370 Seventh Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 Seventh Ave., New York.
Place: Stevens Hotel, Chicago. Time: October 15-19, 1928.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. G. R. Pirie, 20 Madison Ave., Toronto.
Secretary: Dr. A. P. Hart, 1844 Bloor St. West, Toronto.
Place: Vancouver, B. C. Time: June, 1928.

SECTIONAL

CENTRAL STATES PEDIATRIC SOCIETY

President: Dr. H. T. Price, 121 University Place, Pittsburgh.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Ave., Chicago.

SECTION ON PEDIATRICS OF SOUTHERN MEDICAL ASSOCIATION

Chairman: Dr. E. C. Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. A. J. Waring, De Renne Apts., Savannah, Ga.
Place: Asheville, N. C. Time: November 12-15, 1928.

LOCAL

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. W. L. Channell, Medical Bldg., Oakland, Calif.
Secretary: J. E. Parrott, Medico-Dental Bldg., San Francisco.
Place: Various Teaching Schools. Time: Monthly.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Oscar Reiss, Westlake Professional Bldg., Los Angeles.
Secretary: Dr. William Sidney Bowers, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

THE ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. W. Wiley Jones, Majestic Bldg., Denver.
Secretary: Dr. Berryman Green, 537 Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month, 2:30 p. m., September to May, inclusive.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Joseph Yampolsky, 127 Peachtree St., Atlanta.
Secretary: Nevin M. Atkins, Atlanta.
Place: Savannah, Ga. Time: May 9, 1928.

PEDIATRIC SECTION OF FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GA.

President: Dr. William W. Anderson, 362 Peachtree St., Atlanta.
Secretary: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St., Atlanta.
Time: Second Thursday of each month from October to April, at 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. James Herbert Young, 66 Commonwealth Ave., Boston.
Secretary: Dr. Thomas Lanman, 286 Marlborough St., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Maurice Blatt, 30 N. Michigan Ave., Chicago.
Secretary: Dr. J. K. Calvin, 104 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. L. R. De Buys, 1487 Delachaise St., New Orleans.
Secretary: Dr. F. J. Kinberger, 3601 Prytania St., New Orleans.

DETROIT PEDIATRIC SOCIETY

President: Dr. George E. White, Capitol Theatre Bldg., Windsor, Ontario, Canada.
Secretary: Dr. W. S. O'Donnell, 1563 David Whitney Bldg., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. F. W. Schlutz, University of Minnesota, Minneapolis.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: University Campus and Rochester. Time: Winter, Spring, Summer, Fall.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Park J. White, Beaumont Bldg., St. Louis.
Secretary and Treasurer: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

NEBRASKA-IOWA PEDIATRIC SOCIETY

President: Dr. Floyd Clarke, 731 City Nat'l Bank Bldg., Omaha.
Secretary: Dr. R. B. Eldredge, 1036 Medical Arts Bldg., Omaha.
Place: Add-Sell Restaurant. Time: Second Thursday of each month from October to May, inclusive, 6 p. m.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Louis M. Ruderman, 961 Eastern Parkway, Brooklyn.
Secretary: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

BRONX PEDIATRIC SOCIETY

President: Dr. William Hinz, 1964 Grand Concourse, New York.
Secretary: L. H. Barenberg, 1749 Grand Concourse, New York.
Place: Concourse Plaza, 161st, St., and Grand Concourse, New York.
Time: Second Wednesday of each month, except June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady, N. Y.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany, N. Y.
Place: Various Cities in New York. Time: Fourth Thursday of October, January and April.

PEDIATRIC SECTION OF THE NEW YORK ACADEMY OF MEDICINE

President: Dr. William Ropes May, 8 East 66th St., New York.
Secretary: Dr. Stafford McLean, 17 East 71st St., New York.
Place: New York Academy of Medicine, 2 East 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

THE PEDIATRIC SECTION OF THE ACADEMY OF MEDICINE OF CLEVELAND

Chairman: Dr. J. W. Epstein, 3912 Prospect Ave., Cleveland.
Secretary: Dr. Charles W. Burhans, 14805 Detroit Ave., Lakewood, O.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

PEDIATRIC SECTION, ACADEMY OF MEDICINE, TORONTO

President: Dr. M. A. Cox, 34 St. Clair Ave. West, Toronto.
Secretary: Dr. F. R. Hassard, 1361 King St. West, Toronto.
Time: November 17, December 15, February 16 and March 15.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Edward L. Bauer, Jefferson Medical College, Philadelphia.
Secretary: Dr. John Porter Scott, 2040 Pine St., Philadelphia.
Place: College of Physicians, 19 S. 22nd St., Philadelphia. Time: Second Tuesday of each month from October to June, inclusive.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. W. D. Blue, 1024 Madison Ave., Memphis, Tenn.
Secretary: Dr. Gilbert J. Levy, 899 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

TEXAS PEDIATRIC SOCIETY

President: Dr. Lucius D. Hill, Medical Arts Bldg., San Antonio.
Secretary and Treasurer: Dr. Edwin G. Schwarz, Medical Arts Bldg., Fort Worth.
Place: Galveston. Time: May 9, 1928.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Howard Urbach, 1331 Grove Ave., Richmond, Va.
Secretary: Dr. W. Ambrose McGee, West End Medical Bldg., 2618 Grove Ave., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St., Richmond, Va.
Time: First Thursday of each month (other than during the summer).

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Lawrence T. Royster, University, Va.
Secretary: Dr. William B. McIlwaine, Petersburg, Pa.
Place: Danville, Va. Time: October 17, 1928.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. R. S. Miles, Fidelity Bldg., Tacoma, Wash.
Secretary: Dr. D. M. Dayton, 704 St. Helens Ave., Tacoma, Wash.

SEATTLE PEDIATRIC SOCIETY

President: Dr. George B. McCulloch, Cobb Bldg., Seattle.
Secretary: Dr. C. L. Smith, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, at 7 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. A. B. Schwartz, 418 E. North Ave., Milwaukee.
Secretary: Dr. M. G. Peterman, 167 Seventeenth St., Milwaukee.
Place: Children's Hospital, Milwaukee. Time: Second Wednesday of each alternate month, beginning with February.